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American Journal of Diseases of Children

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INTRODUCTION

The literature connected with pedology—the science of the child age—has undergone vast changes since Thomas Thacher's "A Brief Rule to Guide the Common People of New England How to Order Themselves and Theirs in the Small Pocks or Measles" (Jan. 21, 1677-78). This "Broadside," twelve inches by seventeen in size, has been followed by many more broadsides; indeed by roars of broadsides. "The History of American Pediatrics Before 1800," it is true, fills only twenty-five pages of *"Janus,* 1902." It contains, however, mention of the previous and classical treatise of Samuel Bard, "An Enquiry into the Nature, Cause, and Cure of the Angina Suffocativa, or Throat Distemper, as it is commonly called by the Inhabitants of this City and Colony. New York, 1771."

The Nineteenth Century yields a long series of magazine articles and text-books. Dewees, Stewart, Eberle, Condie, Charles D. and Fordyce Meigs were physicians of fame, and their manuals were highly appreciated. Toward the end of the century (1889) W. V. Keating began his five volumes of a "Cyclopedia of the Diseases of Children," which has exerted a great influence in enhancing the taste for the study of healthy and diseased child-life, similar to what C. Gerhardt's epoch-making "Handbuch"—a modest title for a vast achievement—accomplished for Germany since 1877, and Grancher and Comby's "Maladies des Enfants" for France since 1898.

The first systematic instruction in pedology was furnished by the small New York Medical College in East Thirteenth street. In its reorganization of 1860, a full professorship was established. It carried the title of "Infant Pathology and Therapeutics." Subsequent imitations in later times and in other schools of medicine contented themselves with "Pediatrics," the *treating* of children, or the "Diseases of Children," only. The college closed its doors in 1864, during the blights of the Civil War. Meanwhile, the newly founded Bellevue Hospital Medical College organized in 1861 a "Clinical Professorship" for the diseases of children. In

that chair Dr. J. Lewis Smith displayed great industry and enthusiasm, and did much to enlighten the profession in regard to both the difficulties and the importance of the comparatively new doctrine. Another clinical professorship of the same nature was established in 1865 by the University Medical College, and in 1870 by the College of Physicians and Surgeons.

Since that time, the example given by New York has been followed by a large number of the medical schools in the country. Very few of them founded full professorships endowed with the full rights and duties awarded to the rest of the teachers who connected themselves with a medical school or the medical faculty of a university. Harvard was the first to see the light. Though the recognition came late and is far from being universal, we are still ahead of the present status of pedology in the curricula of most European medical schools. Germany, to this day, has few full professorships for instruction in the diseases of children. Indeed, its great teacher and classical writer, Eduard Henoch (1881) closed in 1893 his academic career with the title of a mere "Extraordinary Professor." When, a few weeks ago, however, he was taken away, 90 years old, he had the satisfaction of knowing that there was at last a breach in the short-sighted conservatism of German universities, and that at last a few full chairs of pedology had been established.

Great men like him are scarce in any part of medicine. To excel in close observation, logical reasoning, and elegant and precise diction, together with the faculty of teaching, is given to few men. Charles West in England (1848), Rilliet and Barthez in Switzerland and France (1843), belong to that class and deserve with Henoch the name of classical authors and instructors. They have passed away, but they have been followed by successors, few, it is true, of equal rank, but very numerous and many of them meritorious writers. If but few approach them, the multitude of those who have something to say—and the much greater multitude who say it anyhow—have made the study of the child and its diseases popular and interesting. If it so happens that too much is published, that is only a repetition of the experience of other doctrines in our science and art. Guttenberg's art could not have been discovered by everybody who is satisfied with utilizing or abusing it.

Our present copious pediatric literature dates from about the middle of the last century. Extracts, reviews, and original contributions became

plentiful; our weeklies, monthlies, and quarterlies contained much that was and much that still is of value. The first extensive American papers on diphtheria (1860) and acute rheumatism (1875) were published in magazines. The first volumes of the *American Journal of Obstetrics and the Diseases of Women and Children* (founded in 1869) were almost entirely filled with subjects connected with the anatomy, physiology, and therapeutics of the young. But though the Germans had a special journal since 1843, the first American journal, the *Archives of Pediatrics,* was published by the enthusiastic Watson in 1884 and *Pediatrics* by Dillon Brown in 1896. My readers know that both have rendered good service, both by disseminating knowledge and rousing interest and enthusiasm. At the same time our weeklies have vied with them in supplying the practitioners of the country with information of increasing value.

What all of us have learned is to look on pediatrics not as a specialty, such as ophthalmology or otology, which concern single organs, but as that part of internal medicine and surgery which cannot be measured by the knowledge derived from and applied to the adult; it requires special study and research in order to become both scientific and practical. We learned that there is no uniformity of structure and function in the human organism between conception and death; that childhood must be studied, not from the point of view of reproduction only, but of reproduction *and growth;* that pediatrics does not deal with miniature men and women, with reduced doses and the same class of diseases in smaller bodies, but has its own independent range and horizon, and gives as much to general medicine as it has received from it; that there are anomalies and diseases which are encountered in the infant and child only. On the other hand, there are those which are *mostly* found in children, or with a symptomatology and course peculiar to them; and those, finally, which affect both the young and the old, with such varieties, however, in both symptoms and course, as depend on the size or anatomic structure of the afflicted organ or organism, or the difference in the degree of irritability.[1]

To learn and to teach all that—and many more things—the cooperation of many interests was required. The general practitioner—the majority of whose patients are young—since the belief ceased to be prevalent that the diseases of the small child are "small things," wanted more opportunities to learn than those which his college schooling had pro-

1. Arch. Pediat., November, 1889.

vided for him. The colleges themselves have not been slow in recognizing the advanced condition of pediatrics and the necessities of the physicians of the country.

The increased number of medical magazines—suggested by medical men and published by business men eager to profit by subscriptions and by ethical and unethical advertisements—and text-books—a few excellent, some good, many more, however, mere compilations, most of them with ample sales—have disseminated knowledge which without them would not have been accessible. Even inferior books will convey it and render their owners amenable to the consciousness of their defects and the longing for something more that is not only new but better. For, indeed, the latest is not necessarily the best.

The number of special journals dedicated to pedology or to pediatrics has become quite large. Germany began its oldest and most exclusive *"Journal für Kinderkrankheiten,"* in 1843; it has six or seven such magazines at present; another one appeared lately on account of the large amount of material offered, swamping those in existence. France, England, Spain, Italy, Turkey, and America, all have their special journals. Meanwhile the large weeklies and monthlies have continued to contribute information to those who are interested in pediatrics. In Germany, however, where special pediatric magazines are most numerous and widely appreciated, the pediatric contributions to general journals are becoming less predominant.

The same process of spontaneous exclusiveness will keep on when pediatric journals are published in sufficient numbers and of such a character as to justify and tempt authors to select them for their contributions. But journals are not all of the same standard. Mere compilations will find many grateful readers; a single interesting case accompanied by intelligent culling will prove as acceptable to many a subscriber as it is pleasing to the eye of the writer; discussions in medical societies will frequently add more to the knowledge of a given subject than a labored article on a topic studied up for the instruction, at least, of the author; extracts from the current literature of all nations, particularly when full and systematized, are eagerly sought for and enjoyed.

This new journal of ours, the AMERICAN JOURNAL OF DISEASES OF CHILDREN, however, the first number of which we herewith offer to the profession, is not published to compete with those already in existence.

For some time it has been noted, however, that the pediatric material offered to *The Journal of the American Medical Association* is rapidly increasing in quantity, and also in the size of the articles. Writers were often annoyed by the delay encountered in the publication of their essays; it has even happened that after a delay of many months, authors of the very highest standing were requested to shorten their articles—in many instances an impossible task. Such occurrences suggested the publication of a new special organ. Even those who insisted on the right of the practitioners of the country—members of the Association—to be amply supplied with pediatric teaching by their own journal, receded from the stand taken by them when convinced by the fact that a new journal would not curtail the printing of pediatric contributions in *The Journal of the American Medical Association* and many others of high standing. On the contrary, with the increasing number of physicians interested and working in the field of pedology, there will be more than merely a vast number of papers; there will be more profundity and research. These our new journal is to gather in, and it is to be the companion and ally of the *Archives of Internal Medicine*. It may rarely give a mere case, still more rarely a prescription; it is to be a receptacle, however, of the very latest in the very best of American and European literatures. But extracts will be few in proportion. Reviews, carefully prepared by competent critics, will be offered from time to time. The bulk of the contents, however, will be original; anatomy—both embryonal and postnatal—physiology, biochemistry, nosology, and therapeutics will come to their own, and will be welcomed as our sources of actual progress. Thus, THE AMERICAN JOURNAL OF DISEASES OF CHILDREN is expected to be one of the number of strictly scientific magazines which, since the first appearance of the *Journal of Experimental Medicine* and its followers, have given American medical journalism its standing as an equal coworker in the modern world of Medicine. *Quod felix faustumque sit.*

A. JACOBI.

SOME ANATOMIC FEATURES OF THE CHILD'S THORAX AND THEIR PRACTICAL APPLICATION IN PHYSICAL DIAGNOSIS*

GEORGE FETTEROLF, M.D. AND J. CLAXTON GITTINGS, M.D.
PHILADELPHIA

Since the study of anatomy by means of frozen sections and the use for the same purpose of bodies with the viscera hardened *in situ* have come into vogue, many new ideas have been acquired and many misconceptions corrected. While the study of soft preparations in the dissecting and autopsy rooms has been responsible for almost all our knowledge of gross anatomy, it is not until we examine conditions more nearly as they are during life that we get a really true conception of anatomic relations. The mere opening of the thorax and abdomen under ordinary conditions will of itself cause a change in the shape and relations of the various organs, and when conditions are still further disturbed by dissection or by the successive stages of an autopsy it is possible to get only an approximate idea of conditions as they existed during life.

Our work has consisted of making dissections and of cutting sections of the bodies of infants which had been injected with 10 per cent. dilution of liquor formaldehydi and then frozen. The results of our study of these preparations are embodied in the present paper.

Examination of the child's thorax reveals many important facts, the conception of which is generally inexact. One of these facts is that the thymus body is a structure of considerable size and extent, reaching well beyond the borders of the sternum and separating widely the upper lobes of the two lungs (Figs. 1, 3 and 4). Posteriorly, at least in the first few weeks of life, it extends in places to the trachea (Figs. 2 and 6). It would seem that sudden death at this period, due to respiratory failure, might be caused by even moderate increase in the size of the gland. Delay in the normal involution of this body would extend the danger period.

A point which is very noticeable in the hardened gland is that the upper median portion is deeply indented posteriorly (Fig. 5) by the left innominate vein, which lies immediately on the anterior facies of the

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* From the Laboratory of Anatomy of the University of Pennsylvania.

* Read before the joint meeting of the Pediatric Section of the New York Academy of Medicine and the Philadelphia Pediatric Society, Philadelphia, Nov. 8, 1910.

trachea (Fig. 6). When the size and distensibility of this vessel and the softness and small caliber of the trachea are taken into consideration we have a possible mechanical explanation of the sudden deaths which occur in the young during anesthesia. A slight embarrassment of the right heart or any factor, such as struggling, which would cause a rise of venous pressure, would dilate this vein. Braced firmly on its anterior surface by the thymus, the only direction in which it could extend would be posteriorly and in such an event there would be of necessity compression to a greater or less extent of the trachea. If the amount of compression were great, sudden death would be the result. If of a slighter degree the amount of asphyxia caused by it would tend to raise pressure and cause still further dilatation of the innominate vein, and thus a vicious circle would be established which would soon result in death. If there is any truth in this theory, venesection would be indicated in the emergency.

Another noteworthy point is the amount of space occupied by the heart, which extends at its greatest depth from the sternum to the esophagus, aorta and spinal column (Figs. 7, 8 and 9). In this connection it is evident that a dilated heart or pericardium must exert such marked pressure on the lower third of the upper lobe and the upper two-thirds of the lower lobe of the left lung (Figs. 7 and 8), that in such conditions the frequent presence of bronchial breathing, heard over the back of the chest, is easily accounted for.

It is a well-known fact that in infancy the ribs lie nearly in a horizontal plane and that the sternum occupies a higher position than in the adult, its top lying opposite the body of the first thoracic vertebra.[1] Later in life the sternum drops to a lower plane, owing probably to increase in the size of the lungs, a relative decrease in size of the liver, an actual decrease in size of the thymus and the assumption by the child of the vertical as opposed to the horizontal position.

The internal anatomy of the heart shows many points of interest.

The right auricle lies directly in front of the right half of the left auricle (Fig. 10) but, with the exception of a portion of the appendix (Fig. 9), does not touch the chest wall. The superior vena cava enters the auricle in a plane anterior to that of the inferior cava (Fig. 11). Blood from the latter is directed upward by the Eustachian valve and not to the left, as is commonly supposed. The foramen ovale lies in an almost horizontal plane (Fig. 11), and not vertically and facing to the left. Dextro- or levo-position of the new-born is, therefore, of no importance in aiding the closure of this opening, a point to be elaborated in a future communication.

The tricuspid orifice, an oval ring, is practically vertical (Fig. 12), not horizontal, and opens to the left and slightly forward. The bottom

1. Piersol, George A.: Human Anatomy, 1907, p. 164.

of the right ventricle is so nearly on the level of that of the right auricle (Fig. 12) that gravity must play little if any part in the passing of the blood through the tricuspid orifice. The negative pressure caused by the ventricular diastole and the veno-auricular pressure are the principal factors favoring the rapid filling of the ventricle.

The right ventricle constitutes practically all of the heart which touches the anterior chest wall (Figs. 7 and 12) and is slightly overlapped on each side by the right and left lungs (Fig. 7). Posteriorly it is bounded by two structures, the left ventricle below (Figs. 7 and 15) and the root of the aorta above (Fig. 12). Aortic sounds, therefore, at the level of the second costal cartilage must be heard through the medium of the upper part of the right ventricle, that part known as the infundibulum or conus arteriosus (Figs. 8 and 12), from which arises the pulmonary artery.

The pulmonary artery lies to the left of and slightly anterior to the aorta (Fig. 4) and is separated from the anterior chest wall by the lower portion of the thymus body (Fig. 4). It divides into a long right branch and a short left one. The former runs under the aortic arch and continues along the upper border of the left auricle (Figs. 9 and 12). The left branch passes to the root of the lung across and directly in front of the left bronchus (Fig. 4).

The left auricle is a horizontal cylinder flattened from before backward (Figs. 9 and 12), lying at the extreme back of the heart and extending throughout the entire width of the base of the heart (Fig. 10). It is bounded in front by the right auricle and the left ventricle (Fig. 10), behind by the thoracic aorta (Figs. 9 and 10) and esophagus (Fig. 10), and above by the right pulmonary artery and the left bronchus (Figs. 9 and 12). The right end lies directly behind the right auricle (Fig. 10) and consists of the orifices of the two right pulmonary veins (Fig. 9). At the left end are four openings (Fig. 12). Above and posteriorly are those of the two left pulmonary veins, while above and anteriorly is the opening of the auricular appendix, the two being separated by a practically vertical septum. Below and anterior is the fourth opening, the mitral orifice, which lies in a plane approximately parallel to the anterior facies of the vertebral column (Fig. 12) at this level. The mitral and tricuspid orifices, therefore, lie in planes which are almost at right angles to each other (Fig. 12).

The left ventricle is bounded behind by the left auricle (Fig. 7), and in front, except for the extreme left hand edge, by the right ventricle (Figs. 7 and 13). The two posterior leaflets of the aortic valve are attached to the base of the anterior mitral leaflet (Fig. 12), a fact which furnishes the most plausible theory to account for the mechanism of a "Flint's murmur."

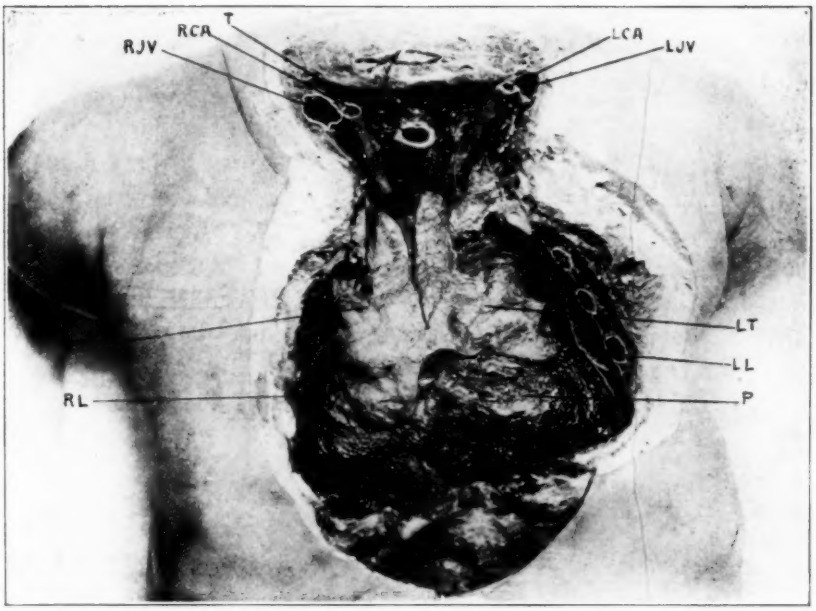

Fig. 1.—Body of a new-born child from which the median portion of the anterior chest wall has been removed. RL, right lung; RT, right lobe of thymus; RJV, right internal jugular vein; RCA, right common carotid artery; T, trachea; LCA, left common carotid artery; LJV, left internal jugular vein; LT, left lobe of thymus; LL, left lung; P, pericardium.

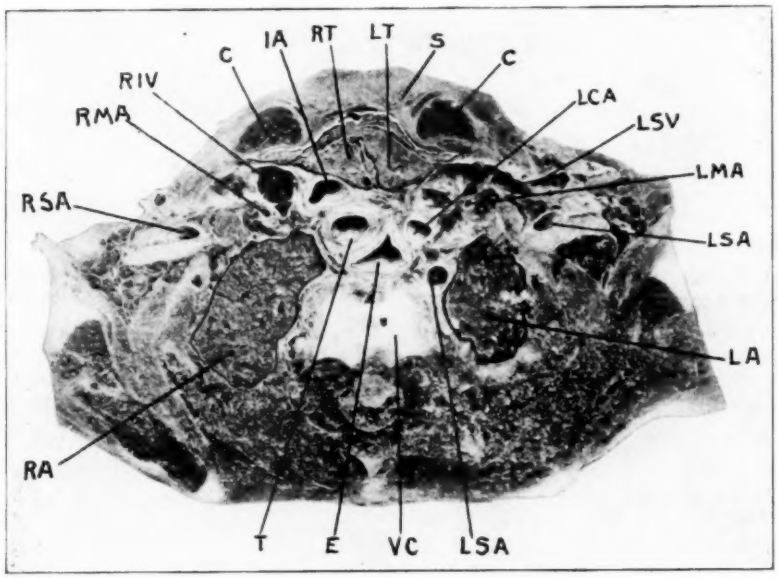

Fig. 2.—Horizontal section, viewed from below, of the body of a new-born child at the level of the upper part of the sterno-clavicular articulation. VC, vertebral column; E, esophagus; T, trachea; RA, apex of right lung; RSA, right subclavian artery; RMA, right internal mammary artery; RIV, right innominate vein; C, C, clavicles; IA, innominate artery; RT, right lobe of thymus; LT, left lobe of thymus; S, sternum; LCA, left common carotid artery; LSV, left subclavian vein; LMA, left internal mammary artery; LSA, LSA, left subclavian artery; LA, apex of left lung.

The arch of the aorta passes almost directly backward (Figs. 4, 9 and 12), instead of from right to left. When it is recognized that the aorta arises from the heart to the left of the midsternal line and descends in the thorax, but slightly to the left of the middle of the vertebral column, this position of the arch is readily understood. In its course backward and very slightly to the left it separates the lower part of the trachea from the adjacent portion of the left lung (Fig. 3), making a distinct arciform groove in the mediastinal facies of the latter organ.

When the heart is considered *in toto* it is seen that the only portions which touch the anterior chest wall are a part of the right auricular

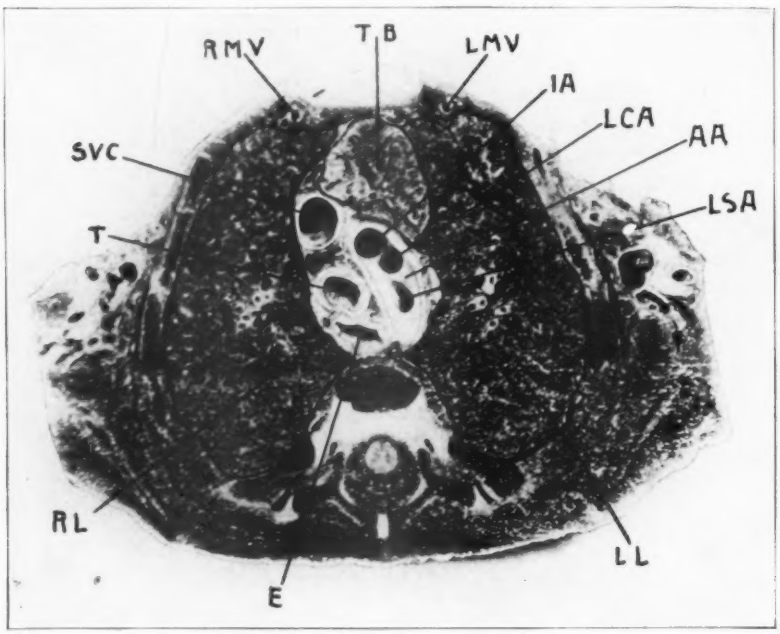

Fig. 3.—Horizontal section, viewed from below, of the body of a new-born child at the level of the upper border of the second rib. E, esophagus; RL, right lung; T, trachea; SVC, superior vena cava; RMV, right internal mammary vessels; TB, thymus body; LMV, left internal mammary vessels; IA, innominate artery; LCA, left common carotid artery; AA, aortic arch; LSA, left subclavian artery; LL, left lung.

appendix and all of the right ventricle, except perhaps the upper part of the infundibulum. The tip of the left ventricle, while it may come into contact with the chest wall, is probably covered by the tip of the lower lobe of the left lung (Fig. 7), that part called the lingula.

Examination of the position of the greater azygos vein (Fig. 11) makes clear the fact that pressure on it by a dilated heart is impossible,

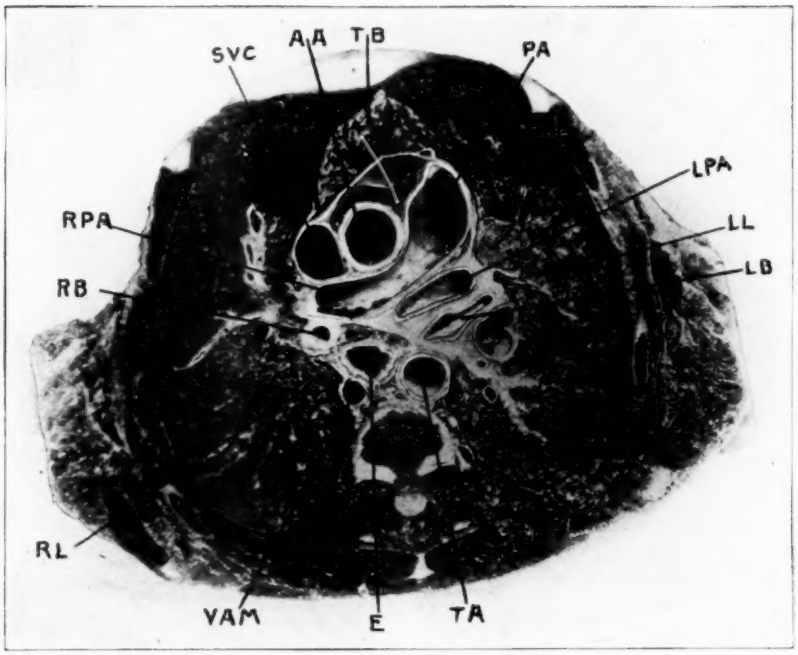

Fig. 4.—Horizontal section, viewed from below, of the body of a new-born child at the level of the upper border of the third rib. E, esophagus; VAM, vena azygos major; RL, right lung; RB, right bronchus; RPA, right pulmonary artery; SVC, superior vena cava; AA, ascending part of aortic arch; TB, thymus body; PA, pulmonary aorta; LPA, left pulmonary artery; LL, left lung; LB, left bronchus; TA, thoracic aorta.

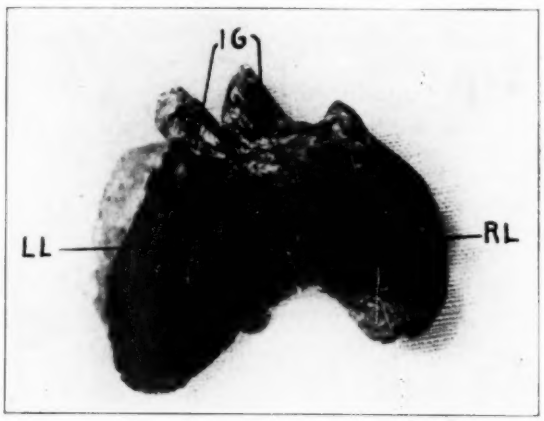

Fig. 5.—Posterior view, life size, of the thymus body of the new-born child depicted in Figs. 1 and 6. LL, left lobe; IG, groove for left innominate vein; RL, right lobe.

whereas pressure on the pulmonary veins, especially the right, can occur with even moderate degrees of cardiac enlargement (Fig. 17). Partial occlusion of these latter veins would explain in large part both the hydrothorax and the pulmonary congestion which are seen in many cases of enlarged heart without signs of stasis in the systemic circuit.

If, in the case of mitral regurgitation, the problem were simply one of overcoming the leakage by the force necessary to pump through the pulmonary artery the normal amount of venous blood, plus the arterial blood, which is returned from the left auricle, the right ventricle would probably be efficient for a long time. From the beginning of mitral leakage, how-

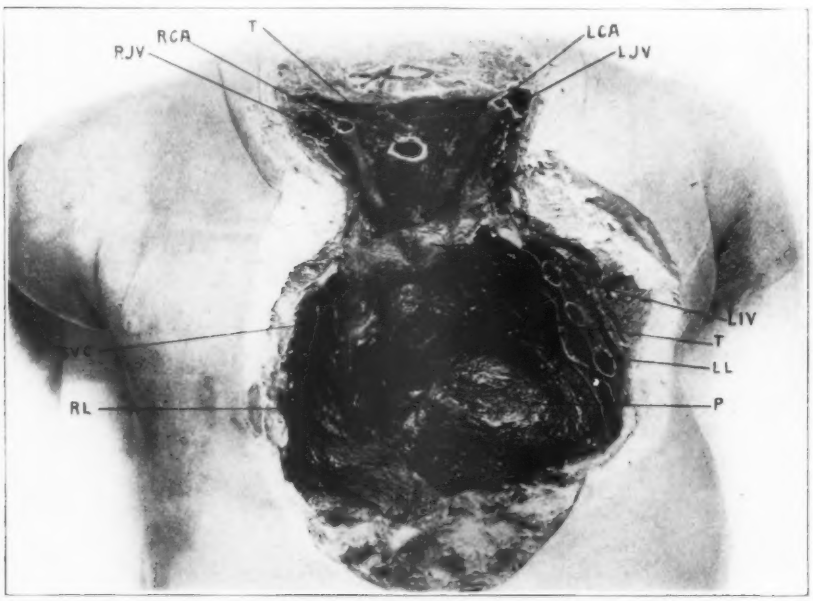

Fig. 6.—Body of the new-born child depicted in Fig. 1, the thymus having been removed. RL, right lung; SVC, superior vena cava; RJV, right internal jugular vein; RCA, right common carotid artery; T, T, trachea; LCA, left common carotid artery; LJV, left internal jugular vein; LIV, left innominate vein; LL, left lung; P, pericardium.

ever, two changes take place, enlargement of the left auricle and, although not quite as early, a similar change in the left ventricle. The former must include enlargement of the appendix as well as of the main cavity, and the appendix, if at all increased in size, is sure to exert pressure on the upper left pulmonary vein, while enlargement of the ventricle would cause pressure on the lower vein (Fig. 18). Compression of these veins at once favors congestion in the radicles, both arterial and venous, in the lung and pleura, the veins of the human pleura opening as they do into

the pulmonary veins,[2] so that the right ventricle has to overcome both this congestion and the back flow which takes place during systole of the left ventricle. In the same manner enlargement of the right auricle causes pressure on the right pulmonary veins (Fig. 17), and it seems to us highly probable that it is this factor of pressure on the pulmonary veins[3] which aids materially in producing pulmonary congestion and pleural leakage, as well as in promoting failure of competence of the right side of the heart.

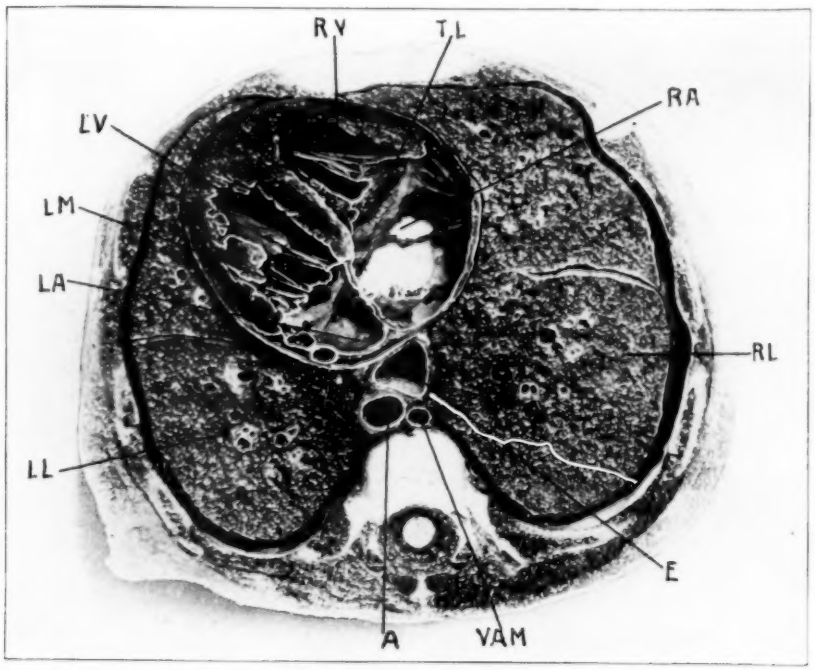

Fig. 7.—Horizontal section, viewed from above, of the body of a new-born child at the level of the upper border of the fifth rib. A, thoracic aorta; LL, left lung; LA, left auricle; LM, mitral leaflet; LV, left ventricle; RV, right ventricle; TL, tricuspid leaflet; RA, right auricle; RL, right lung; E, esophagus; VAM, vena azygos major.

The relatively loud sound of the closure of the pulmonary valve in children, as compared with that of the aortic, may be due in part to the fact that the upper lobe of the left lung does not cover the pulmonary artery (Fig. 16) as well as in adults and possibly to the presence of the thymus (Fig. 16), which would furnish a good conducting medium from

2. Miller, W. S.: Am. Jour. Anat., vii, 404, 405.
3. Fetterolf and Landis: Am. Jour. Med. Sc., November, 1909.

valve to chest wall. More important, however, is the physiologic difference in systemic tension between child and adult.

From a correct conception of the position of the heart *in vivo* we may draw conclusions as to the pathologic anatomy in case of enlargement. Increase in size to the left would be due mainly to enlargement of the left ventricle (Fig. 7); to the left and upward mainly to the left auricular appendix (Fig. 18) and to a slight extent the left auricle (Fig. 10); to the left and downward to the left and right ventricles (Figs. 7 and 13). Enlargement to the right would involve mainly the right auricle

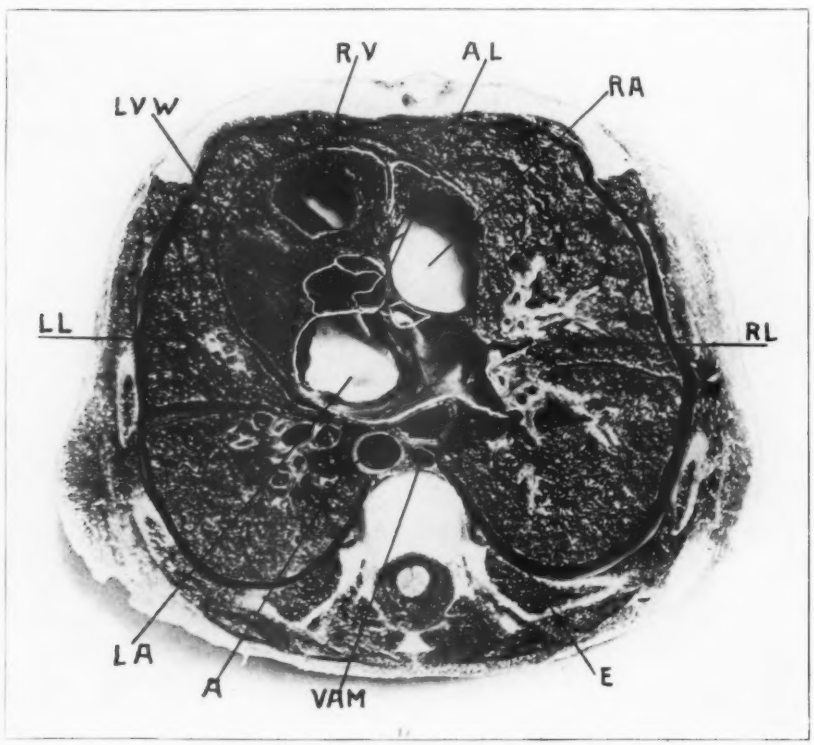

Fig. 8.—Horizontal section, viewed from above, of the body of a new-born child at the level of the upper border of the fourth rib. VAM, vena azygos major; A, aorta; LA, left auricle; LL, left lung; LVW, left ventricular wall; RV, right ventricle; AL, aortic leaflet; RA, right auricle; RL, right lung; E, esophagus.

and appendix (Fig. 11), and to a lesser extent the right ventricle and the right end of the left auricle (Fig. 11).

A noteworthy point is that the mitral, tricuspid and aortic valves are practically contiguous structures (Fig. 12). This readily explains the difficulty in distinguishing the murmurs produced in cases of double or

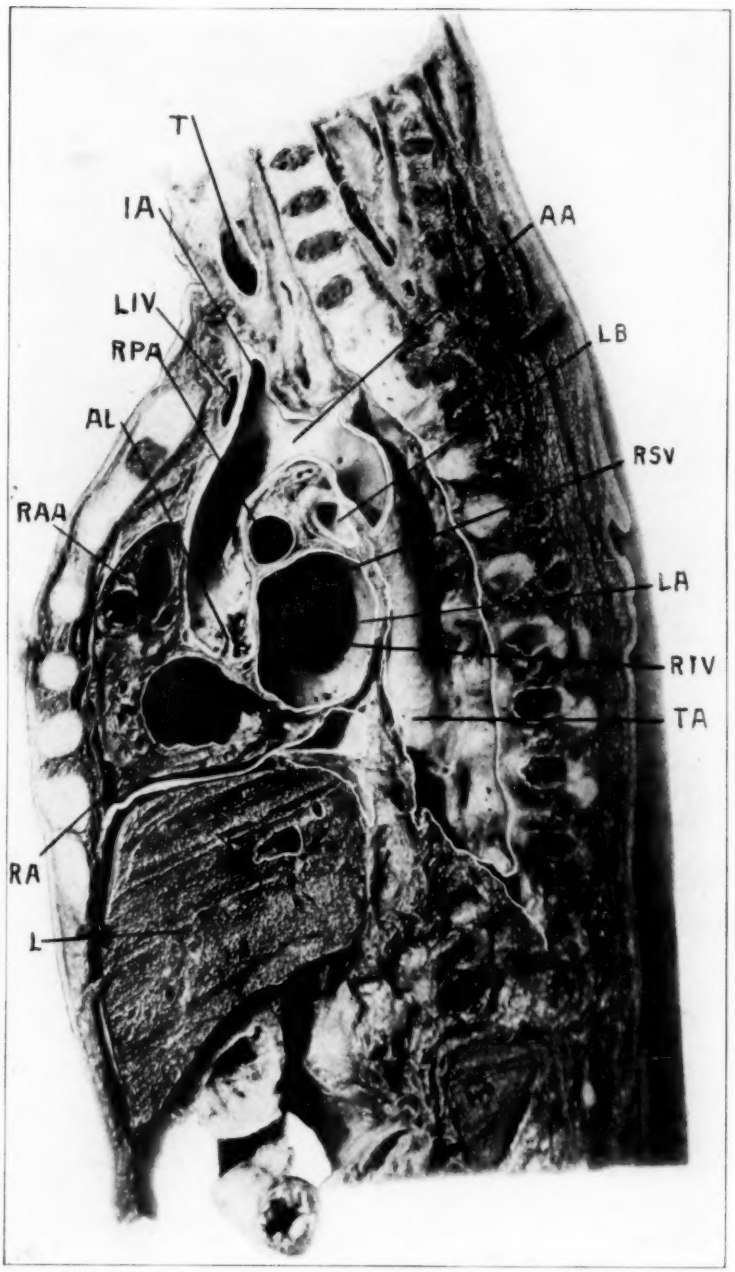

Fig. 9.—Sagittal section, viewed from the left, of the body of a new-born child, the plane of section being 0.75 cm. to the left of the midsternal line. L, liver; RA, right auricle; RAA, right auricular appendix; AL, aortic leaflets; RPA, right pulmonary artery; LIV, left innominate vein; IA, innominate artery; T, trachea; AA, aortic arch; LB, left bronchus; RSV, right superior pulmonary vein; LA, left auricle; RIV, right inferior pulmonary vein; TA, thoracic aorta.

triple lesions or leakage. When we add to this the ease with which cardiac sounds, both normal and abnormal, can be heard in children, owing principally to the thinness of the chest wall, it would appear that a differentiation between a mitral and a tricuspid regurgitation, for example, would be impossible from the murmurs alone. A systolic murmur heard in the left axilla but not in the carotids or right axilla, would indicate mitral regurgitation. An aortic systolic murmur can be diagnosed with certainty only in the neck, while a systolic murmur heard over the heart, but not in the left axilla or in the neck, would point more strongly to a

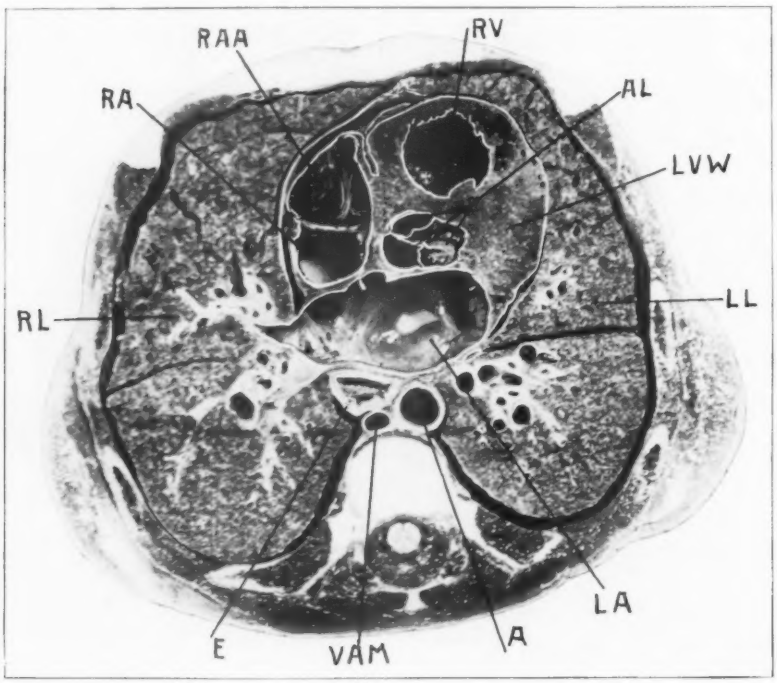

Fig. 10.—Horizontal section, viewed from below, of the body of a new-born child at the level of the upper border of the fourth rib. VAM, vena azygos major; E, esophagus; RL, right lung; RA, right auricle; RAA, right auricular appendix; RV, right ventricle; AL, aortic leaflets; LVW, left ventricular wall; LL, left lung; LA, left auricle; A, aorta.

functional cause than to tricuspid regurgitation. A pure diastolic murmur heard anywhere over the heart is usually due to aortic regurgitation.

Some interesting features in regard to the lungs have been noted. Everyone is familiar with the normal relative differences between the physical signs over the right and left apices. Various explanations have

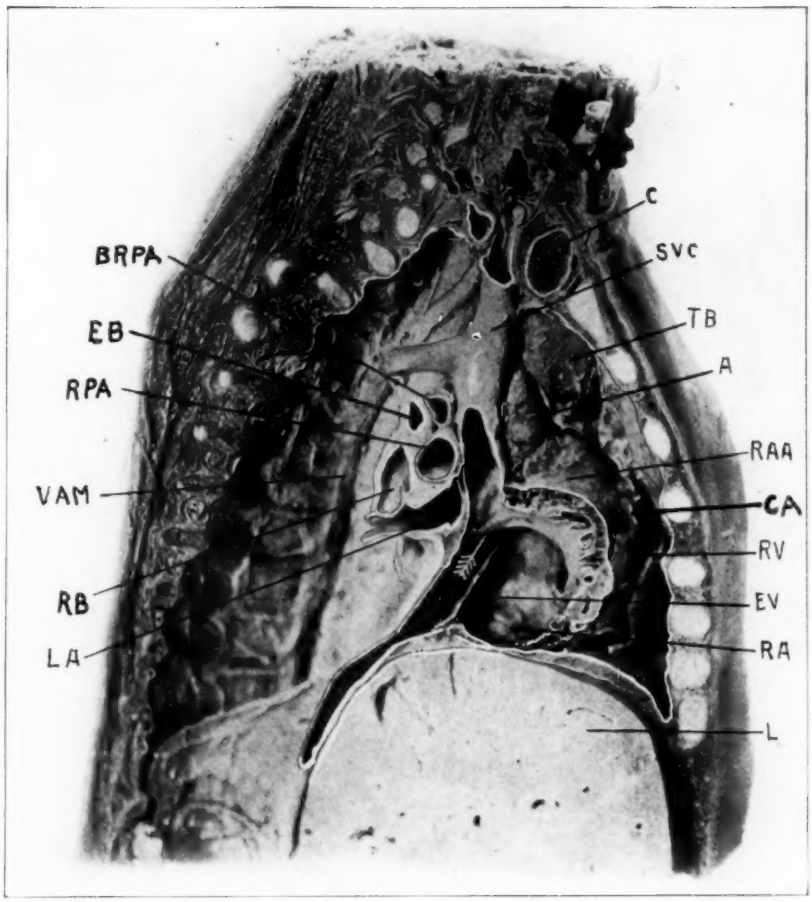

Fig. 11.—Sagittal section, viewed from the right, of the body of a new-born child, the plane of section being 0.75 cm. to the right of the midsternal line. LA, left auricle; RB, right bronchus; VAM, vena azygos major; RPA, right pulmonary artery; EB, eparterial bronchus; BRPA, branch of right pulmonary artery; C, clavicle; SVC, superior vena cava; TB, thymus body; A, root of aorta; RAA, right auricular appendix; CA, conus arteriosus; RV, right ventricle; EV, Eustachian valve; RA, right auricle; L, liver. The arrow is in the foramen ovale.

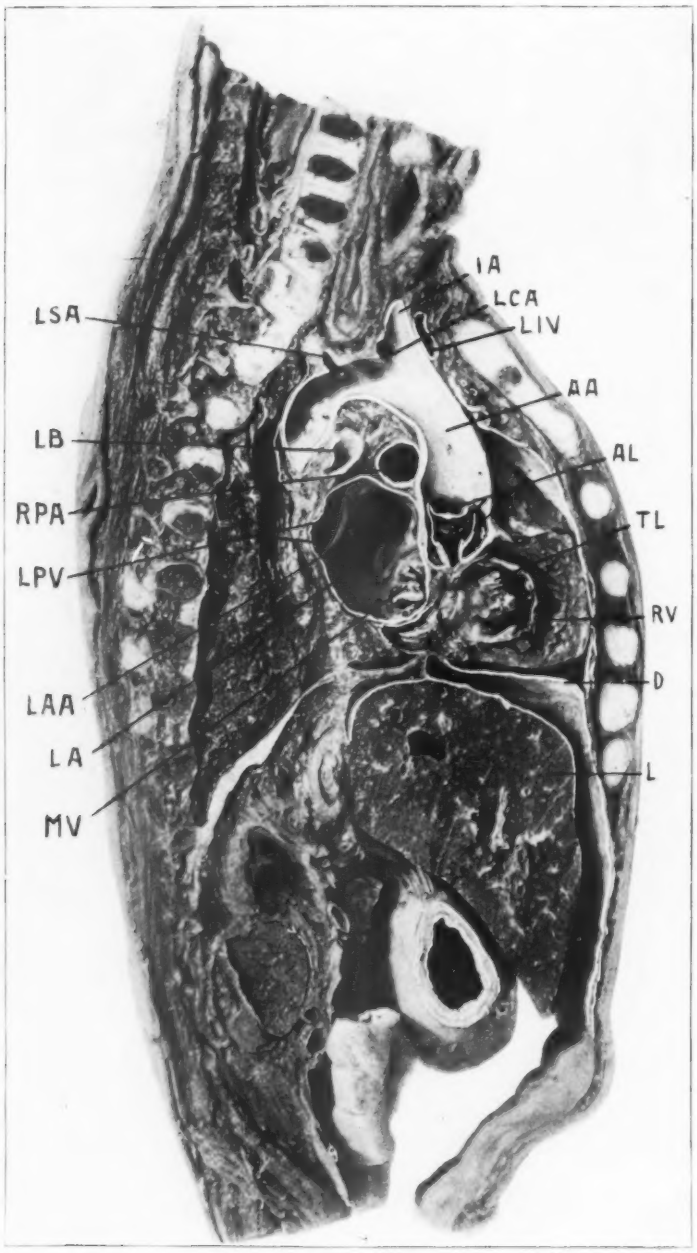

Fig. 12.—Sagittal section, viewed from the right, of the body of a new-born child, the plane of section being 0.75 cm. to the left of the midsternal line. MV, mitral valve; LA, left auricle; LAA, left auricular appendix; LPV, orifices of left pulmonary veins; RPA, right pulmonary artery; LB, left bronchus; LSA, left subclavian artery; IA, innominate artery; LCA, left common carotid artery; LIV, left innominate vein; AA, aortic arch; AL, aortic leaflets; TL, tricuspid leaflets; RV, right ventricle; D, diaphragm; L, liver.

been offered from time to time but the one pointed out by one of us[4] is shown clearly in our preparations. This explanation rests on the anatomic relations of the trachea and the pulmonary apices. On the right side they are absolutely contiguous structures (Fig. 2), while on the left they are separated by the aorta, the left carotid and subclavian arteries, the esophagus and some areolar and lymphoid tissue (Fig. 2). In this connection should be mentioned the dulness to the left of the upper sternum to which attention has been called by Hamill and LeBoutillier.[5] This is probably due partly to the facts just mentioned, partly to the exposure of

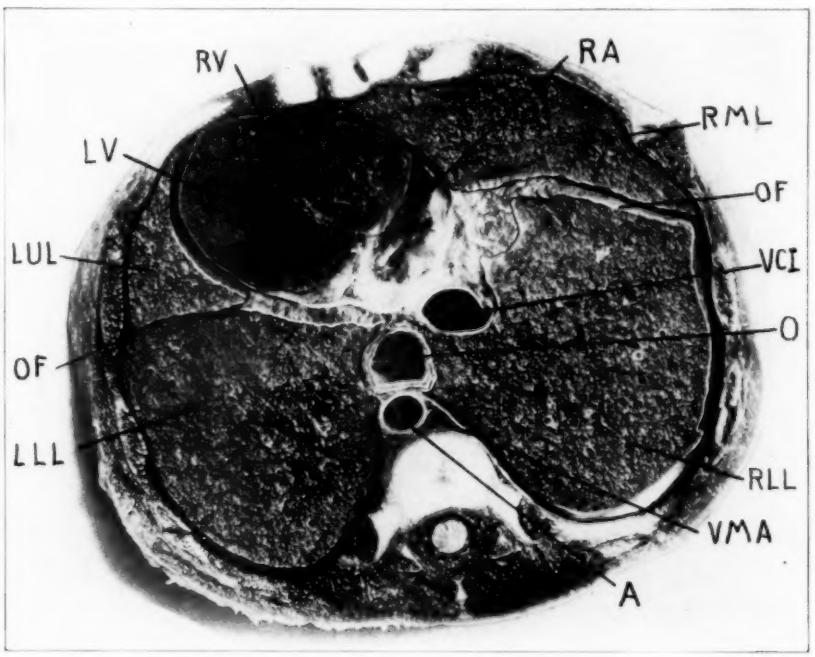

Fig. 13.—Horizontal section, viewed from above, of the body of a new-born child at the level of the upper portion of the ensiform cartilage. LLL, lower lobe of left lung; OF, oblique fissure of left and right lungs; LUL, upper lobe of left lung; LV, left ventricle; RV, right ventricle; RA, right auricle; RML, middle lobe of right lung; VCI, vena cava inferior; O, esophagus; RLL, lower lobe of right lung; VMA, vena azygos major; A, aorta.

the pulmonary artery on account of the posterior position of the anterior margin of the left lung as compared with the adult, and partly to the

4. Fetterolf, George: The Anatomic Explanation of the Greater Amount of Vocal Fremitus and Vocal Resonance Normally Found at the Apex of the Right Lung, Arch. Int. Med., February, 1909, p. 23.

5. Hamill, Samuel McC., and LeBoutillier, Theodore: Some Physical Signs in Infants and Children Not Sufficiently Emphasized, Jour. Am. Med. Assn., Jan. 7, 1905, p. 26.

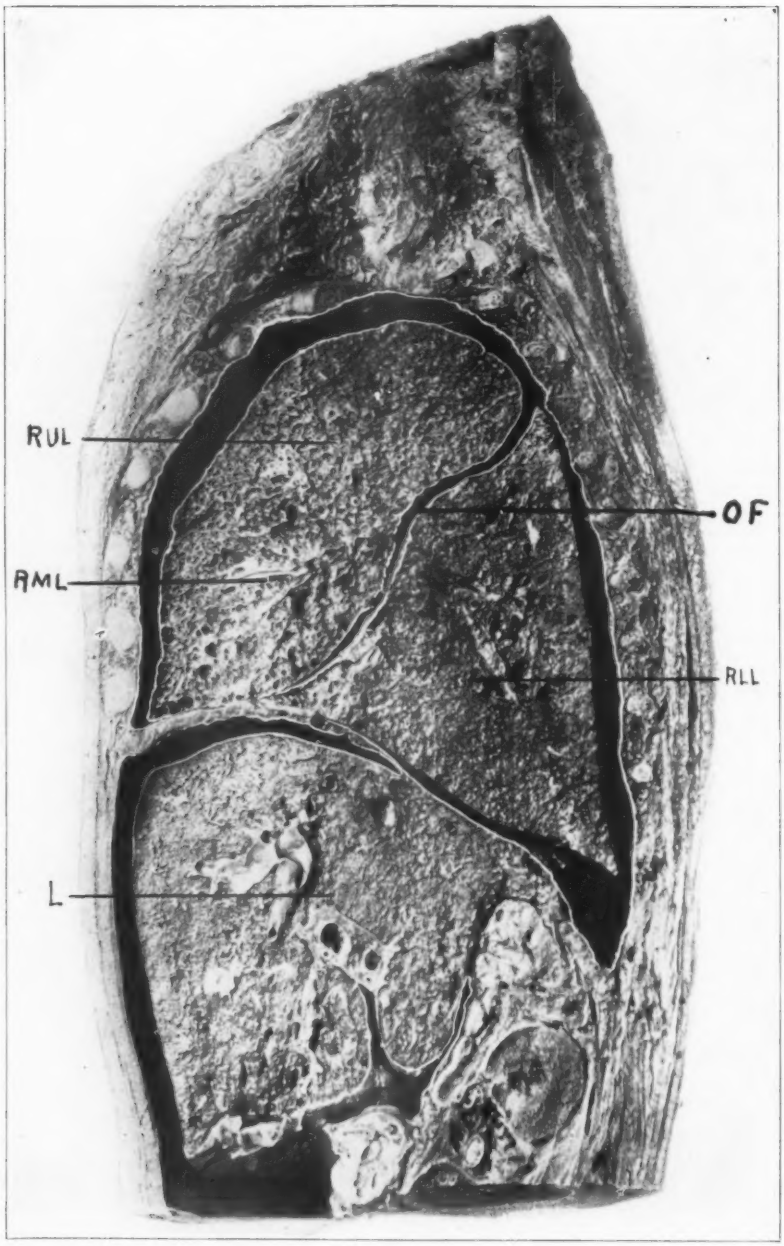

Fig. 14.—Sagittal section, viewed from the left, of the body of a new-born child, the plane of section being 2 cm. to the right of the midsternal line. Owing to adhesions the horizontal fissure is not shown. L, liver; RML, middle lobe of right lung; RUL, upper lobe of right lung; OF, oblique fissure; RLL, lower lobe of right lung.

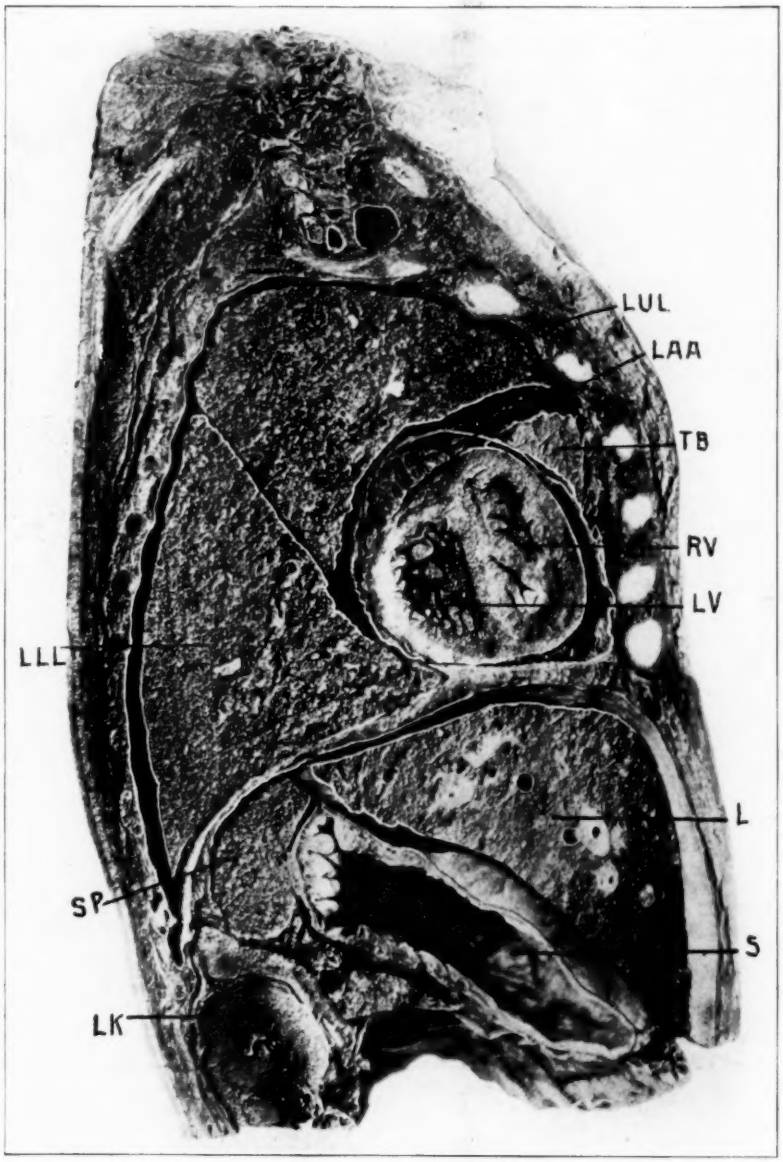

Fig. 15.—Sagittal section, viewed from the right, of the body of a new-born child, the plane of section being 2 cm. to the left of the midsternal line. LK, left kidney; SP, spleen; LLL, lower lobe of left lung; LUL, upper lobe of left lung; LAA, left auricular appendix; TB, thymus body; RV, right ventricle; LV, left ventricle; L, liver; S, stomach.

greater extent of the left lobe of the thymus (Fig. 1). In addition, the left lobe of the thymus is backed by a mass of solid tissue interposed between the left upper lobe and the trachea, while the right lobe is backed by resonating tissue in the shape of the right upper pulmonary lobe.

The high position of the dome of the liver on the right side is clearly demonstrated (Figs. 11 and 14) and explains the high-pitched or relatively dull note which is heard in percussing over the right pulmonary base. On the left side the spleen is seen to reach a level almost as high as that of the liver, the difference being not more than that of a rib and interspace.

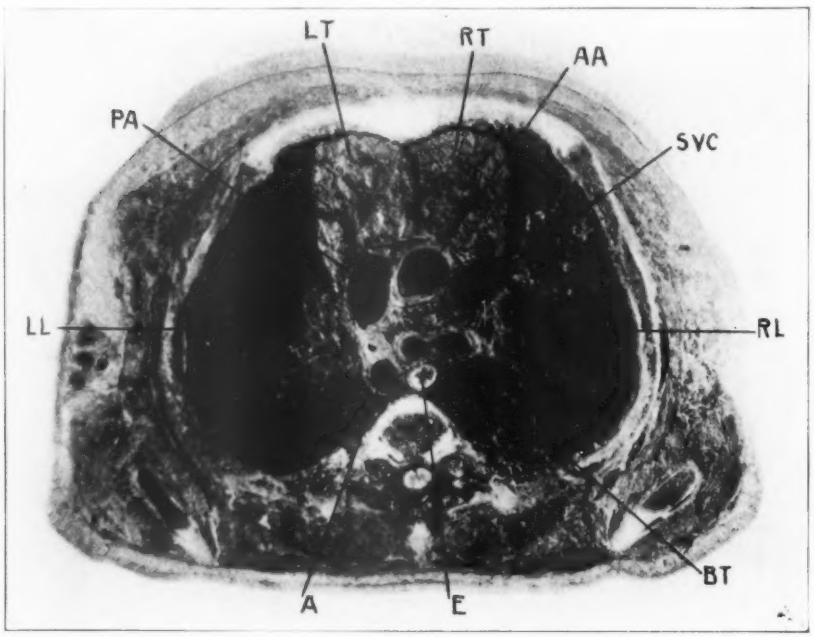

Fig. 16.—Horizontal section, viewed from above, of the body of a new-born child at the level of the upper border of the third rib. LL, left lung; PA, pulmonary aorta; LT, left lobe and RT, right lobe of thymus body; AA, ascending part of aortic arch; SVC, superior vena cava; RL, right lung; BT, bifurcation of trachea; E, esophagus; A, descending part of aortic arch.

The edge of the lung which overlaps the right border of the heart is so thin (Fig. 10) that it should hardly interfere with a reasonably accurate determination of the right border of cardiac dulness.

The position of the bronchial lymph nodes at the bifurcation of the trachea (Fig. 16) is so far above the heart, which would furnish a conducting medium, that it is difficult to conceive how enlargement of these nodes could produce a bruit, even on forced extension of the head, which

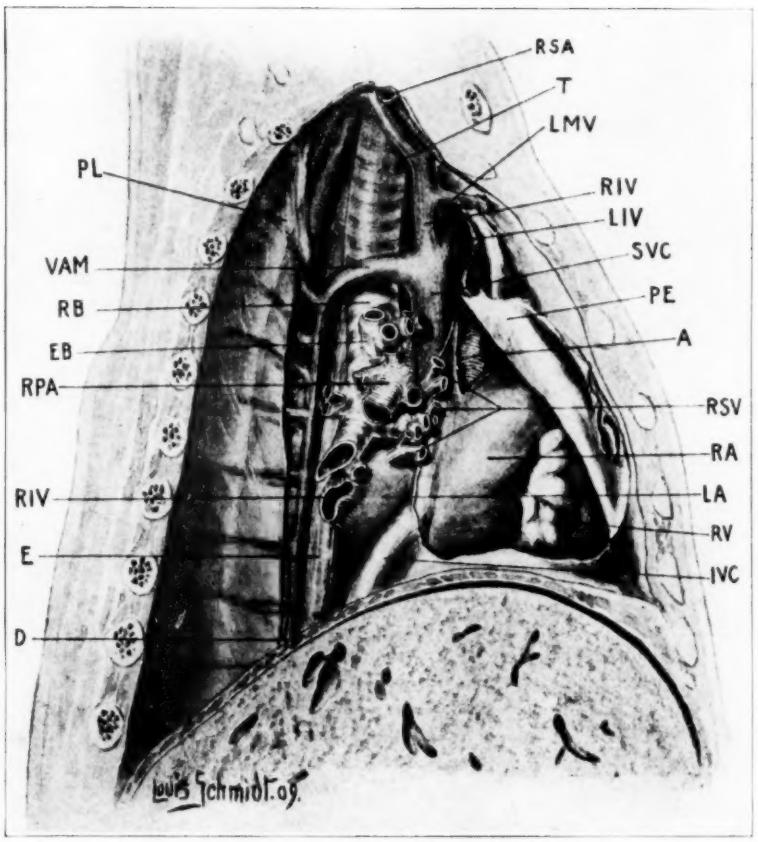

Fig. 17.—View from the right of the mediastinal contents and the root of the lung of the body of a 6-months-old child. D, diaphragm; E, esophagus; RIV, right inferior pulmonary vein; RPA, right pulmonary artery; EB, eparterial bronchus; RB, right bronchus; VAM, vena azygos major; PL, pleura; RSA, right subclavian artery; T, trachea; LMV, right internal mammary vein; RIV, right innominate vein; LIV, left innominate vein; SVC, superior vena cava; PE, pericardium; A, aorta; RSV, right superior pulmonary vein; RA, right auricle; LA, left auricle; RV, right ventricle; IVC, inferior vena cava. (Fetterolf and Landis: *Am. Jour. Med. Sc.*, November, 1909.)

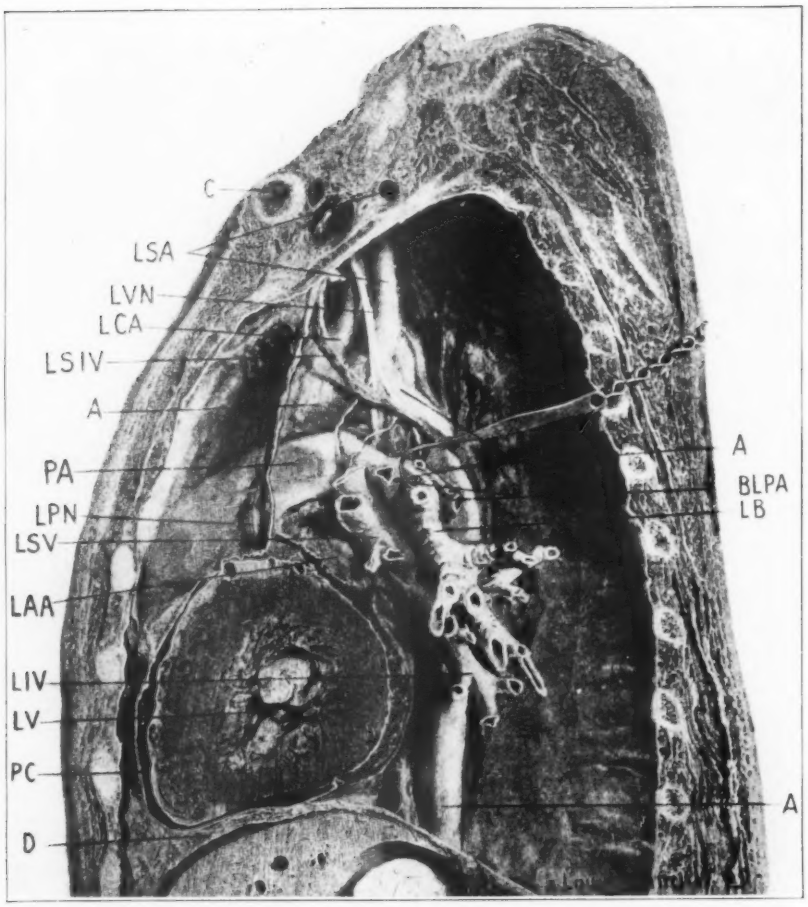

Fig. 18.—View from the left of the mediastinal contents and root of the left lung of the body of an adult. D, diaphragm; PC, pericardial chamber; LV, left ventricle; LIV, left inferior pulmonary vein; LAA, left auricular appendix; LSV, left superior pulmonary vein; LPN, left phrenic nerve; PA, pulmonary aorta; A, aorta; LSIV, left superior intercostal vein; LCA, left common carotid artery; LVN, left vagus nerve; LSA, left subclavian artery; C, clavicle; A, A, A, aorta; BLPA, branch of left pulmonary artery; LB, left bronchus. (Fetterolf and Landis: *Am. Jour. Med. Sc.*, November, 1909.) This section, while that of an adult, shows the points under discussion so well that it is used in preference to preparing a new dissection of an infant.

could be heard over the upper sternum. The explanation of this bruit would seem to depend rather on the persistence of the thymus, which could exert pressure on the vessels as they arise from the arch of the aorta (Fig. 3).

Since the bronchial nodes are surrounded by so many other structures which would give a dull note on percussion, such as the arch of the aorta, the great vessels, and the thymus, it seems to us highly problematical that enlargement of these nodes can be accurately diagnosed by percussion.

Finally, the sections afford a clear demonstration of the position of the lobes of the lungs and emphasize the fact that physical signs in the lungs posteriorly, as high as the base of the spines of the scapulæ, are produced in the lower lobes (Figs. 14 and 15). Anteriorly, on the right, the fourth rib divides the upper from the middle lobe, while on the left any signs heard above the heart and in front of the anterior axillary line would denote that the upper lobe is affected.

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OBSERVATIONS ON THREE HUNDRED CASES OF ACUTE MENINGITIS IN INFANTS AND YOUNG CHILDREN

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NEW YORK

With the introduction of lumbar puncture the diagnosis of acute meningitis entered on a new phase. This is quite as important an advance in this group of diseases as was the adoption of throat cultures in diphtheria and other throat affections. Exact diagnosis has now become possible where formerly in very many cases only a probable diagnosis could be made. The period during which lumbar puncture has been systematically performed on all suspected cases in the Babies' Hospital covers the last five years.

The observations included in this paper relate to 300 cases of acute meningitis seen in this hospital, in children for the most part under three years of age. Of this number 197 have been observed during the lumbar puncture period and are available for more careful analysis. Some valuable data obtained from the records of 103 earlier cases are introduced. In order to gain some idea of the relative frequency of the different forms of acute meningitis I have not included in the table cases seen before lumbar punctures were regularly made nor cases of cerebrospinal meningitis observed during the epidemic which ended in the spring of 1906, so that I think the figures which follow may be taken as fairly representing the usual conditions.

Etiologically, the 197 cases are divided as follows:

Tuberculous	138
Pneumococcus	22
Meningococcus (sporadic)	24
Staphylococcus or streptococcus	10
Bacillus influenzæ	4
Colon bacillus	1
	199
Counted twice, mixed infections	2
	197

In other words, apart from epidemics of cerebrospinal meningitis, 70 per cent. of the cases of acute meningitis occurring in young children are tuberculous. The objection may perhaps be raised that hospital figures are not to be taken as representing conditions which obtain generally. The admissions to the Babies' Hospital are, however, from every class, and I think this criticism will not hold.

During the last five years lumbar puncture has been performed about one thousand times. After simple lumbar puncture no accidents have occurred; there have been no alarming symptoms, and no case of infection. However, in a single instance in which repeated injections were made in a case of cerebrospinal meningitis for the injection of Flexner's serum, secondary infection did occur, in spite of routine aseptic precautions. This is a warning which should be heeded. In another child suffering from cerebrospinal meningitis an alarming collapse followed the injection of 35 c.c. of serum. The fluid was warmed and the injection made in the usual manner, but the child came near dying and was rescued only after the most strenuous efforts. Aside from these two cases my experience has been without special incident. Too much, therefore, can hardly be said in favor of a systematic resort to lumbar puncture as a means of diagnosis in cases of meningitis; but it is a procedure requiring considerable skill and necessitating as strict asepsis as any surgical operation.

SIMPLE MENINGITIS

Before passing to a consideration of the different groups of cases which have been enumerated, I should like to say a word concerning "simple meningitis," a term formerly much used and one which still figures largely in vital statistics. In most such reports three forms of meningitis are given: tuberculous, cerebrospinal and simple. Some give only tuberculous as a separate class, combining cerebrospinal and simple. In the U. S. Census Report of the registration area for 1908 there are mentioned 71,229 deaths from meningitis in the five years 1904-1908; 25 per cent. of these are classed as cerebrospinal; 26 per cent. as tuberculous, and 49 per cent. as "simple or unqualified." In this same report, of 6,902 cases of meningitis occurring in the first three years of life in the year 1908, 32 per cent. are classed as tuberculous. In the New York City report for 1908 there are recorded in children during the first three years of life, 819 deaths from meningitis, divided as follows:

Tuberculous	448 or 55 per cent.
Cerebrospinal	188 or 23 per cent.
Simple	183 or 22 per cent.

Previous to the period here considered the diagnosis of "simple meningitis" appears in the hospital records in twenty-three cases. It was at that time our custom to contrast such cases with those which were tuberculous. At present the group "non-tuberculous" meningitis has been pretty well differentiated. The term "simple meningitis" has no longer any significance and should be dropped. There is not the slightest doubt that the largest proportion of cases so classified belong in the tuberculous group. From experience in the hospital, where careful differential diagnosis of the different forms of meningitis has been possible by lumbar

puncture, it is evident that tuberculous meningitis is very much more frequent than would appear from vital statistics of the country generally, or even those of New York City, and that a large number, probably the great majority of the cases put down as simple meningitis, and many of those recorded as cerebrospinal, are really tuberculous.

COLON MENINGITIS

Beginning with the smallest group I wish first to mention a case of meningitis due to a bacillus of the colon group which occurred in a baby only four weeks old. The child was admitted for an Erb's palsy and malnutrition. The usual symptoms of meningitis developed: temperature up to 103 F., leukocytosis of 13,000, general hyperesthesia and rigidity. A purulent fluid was drawn by lumbar puncture which showed a pure growth of a bacillus of the colon group. The illness lasted ten days. There were no symptoms pointing to visceral lesions elsewhere, but no autopsy could be obtained. In private practice I have seen one other case of meningitis in which the only growth from the cerebrospinal fluid was a bacillus of the colon group. This also occurred in an infant four weeks old, who had previously suffered, it was reported, from a urinary infection due to the colon bacillus. The child recovered from the acute symptoms, but developed a secondary hydrocephalus.

INFLUENZA MENINGITIS

Thus far four cases of meningitis due to the *Bacillus influenzæ* have been observed; all of which have occurred during the last year. Clinically this form resembles the meningococcus cases and it is only by lumbar puncture that a differential diagnosis can be made. These cases are not common. I have seen but one other in private practice. Dr. Flexner tells me that he has had a considerable number of fluids sent to him with clinical diagnosis of cerebrospinal meningitis which contained only the influenza organism. All these ended fatally, as well as those which have been personally seen. It is my belief that this is the almost invariable termination. In three of the four cases that have come under my observation the *B. influenzæ* was obtained by cultures from the bronchial secretion during life, and in two, in which examinations were made, it was also obtained by culture from the nasopharynx. This would suggest the nasal mucosa as the port of entry. In three cases examined the organism was found in the blood. One recent case had some features of unusual interest. An infant of eight months was admitted to the hospital with an acute abscess of the left elbow. Cultures from the pus on ordinary media gave no growth; however, on blood-agar a pure growth of the *B. influenzæ* was obtained. The child shortly after developed acute men-

ingitis and died from the disease. The cerebrospinal fluid during life and the cultures from the meningeal exudate at autopsy showed a pure growth of the *B. influenzæ*.

MENINGITIS FROM PYOGENIC ORGANISMS

The common pyogenic organisms, streptococcus and staphylococcus, have been very infrequently found by me as the cause of meningitis. They were present in but ten cases. In one other a streptococcus infection complicated a tuberculous case. It is rather striking that six of the ten cases occurred in newly-born children, and that in five the meningitis was secondary to spina bifida. In one it followed an operation on a hydrocephalus, and in only two cases did it occur under conditions resembling a primary inflammation. In one case, in an infant three months old, the autopsy showed encephalitis as well, and the streptococcus was also found in the heart's blood and lungs.

Clinically this form of meningitis was characterized by severe general and local symptoms and a rather rapid development, with always an unfavorable termination. Since so much has been made in medical literature of the association of otitis media and mastoiditis with acute meningitis, my experience on this point may possess some interest. I saw meningitis develop but once after otitis or its complications. This patient was a baby fifteen months old who had had a double mastoid operation done in Europe. Dressings had not been changed from the time the child had sailed until she was admitted to the hospital, a period of nearly two weeks. At that time they were very foul and the wound in bad condition, and the child desperately ill. Symptoms of acute meningitis developed and the child died in the course of a few days. The autopsy, however, showed the meningitis to be a tuberculous one. A careful examination showed no connection whatever between the mastoid lesion and the one in the meninges. My experience leads me to question whether the dangers of meningitis from cases of otitis or mastoiditis are as great as they have been represented. I have always in the hospital wards many cases of acute otitis and a moderate number of these patients develop mastoid complications. However, on by no means all of them is the mastoid operation done. I am, therefore, led to the opinion that so far as patients of this age, chiefly under two years, are concerned, meningitis from a neglect to perform the mastoid operation is one of the rarest occurrences.

MENINGOCOCCUS MENINGITIS

It is not my purpose to enter minutely into a study of the twenty-four sporadic cases of cerebrospinal meningitis which have occurred since the great epidemic nearly five years ago. The number is too small to admit of any generalizations. Fourteen children received serum treatment, of

whom six recovered and eight died. The deaths included one chronic case in which the patient was injected in the third month when in a hopeless condition. Another was one of the first patients to be treated by the serum; in this case only a single small dose was administered. One child was improving but died from intercurrent measles. Two children, one an infant of five weeks and another of nine months, died of marasmus after all symptoms of acute meningitis had subsided. One child at first improved very much under the injection of the serum, and all the organisms disappeared from the fluid, but the child steadily lost ground and died, the autopsy showing an encapsulated meningeal abscess at the convexity, containing fully half an ounce of pus which, by culture, showed the meningococcus. One child died suddenly a week after all acute symptoms had passed. No autopsy could be obtained. Death in one instance was due to secondary infection with the staphylococcus.

In several of our cases which ended in recovery the nervous symptoms were slow in disappearing. Inability to support the head sometimes existed for two or three months, and in two cases evidence of a moderate intraventricular effusion persisted for several weeks, but finally disappeared. I have been struck with the irregularity exhibited by these cases in infants, by the slowness of recovery and by the large doses of the serum required in those who did get well.

Of ten patients who received no serum, three recovered and six died; one was discharged unimproved and doubtless died soon after.

PNEUMOCOCCUS MENINGITIS

Twenty-two cases of pneumococcus meningitis were observed, or about 11 per cent. of the entire number. Of these, thirteen patients had definite pneumonia with consolidation and four of these had also empyema. One patient had pulmonary tuberculosis. Of the eight remaining patients nearly all had some pulmonary signs and symptoms, evidences of bronchitis at least. The diagnosis was confirmed by autopsy in eleven of the twenty-two cases. In twenty the pneumococcus was found in the cerebrospinal fluid; one of the two remaining cases coming to autopsy.

The histories of the two patients in whom lumbar puncture gave negative results have already been published[1] but are sufficiently interesting to refer to again. While in only one of these was the diagnosis established by an autopsy, the symptoms in the second case were so similar that the diagnosis seems reasonably clear, though not positively proven.

The first was a child 20 months old whose attack came on with repeated convulsions, fever and a leukocytosis of 24,000. For one week the symptoms were those of a fairly typical acute cerebrospinal meningitis except for the absence of rigidity of the neck and extremities. Puncture made on the first day and repeated on the seventh day gave a perfectly

1. Arch. Pediat., March, 1908.

clear fluid. No organisms of any kind could be discovered in the smears or by culture. During the third week the patient developed pneumonia with consolidation; and the persistence of the nervous symptoms led to a third puncture which, like the other two, gave negative results although the amount of fluid removed was large—105 c.c. After six weeks all the acute symptoms subsided and the condition resembled one of a mentally defective child with slow wasting. Death occurred in the eleventh week from a second attack of pneumonia. The autopsy showed an old meningitis at the convexity; from this exudate a pure growth of the pneumococcus was obtained. The base of the brain was normal.

The second case occurring in a child 15 months old was almost the counterpart of this first one, but ended in partial recovery. Three punctures were made, in all of which the fluid was negative. Pneumonia developed in the fourth week but cleared up. Active nervous symptoms continued for four weeks, then gradually passed away. When discharged from the hospital the patient could not sit up nor support the head. Vision and hearing seemed absent. Six months later the patient was seen again. There had been considerable improvement, but the child clearly was mentally defective.

It seems evident that there was in both of these cases some involvement of the cortex in the inflammatory process; but no paralysis occurred in either case. Neither in its symptoms nor in its course did the disease suggest the cerebral form of poliomyelitis. We are accustomed to place so much reliance on lumbar puncture that the possibility of the existence of acute meningitis with a normal fluid is rather difficult to grasp.

Clinically, pneumococcus meningitis is shorter than any of the other forms, possibly excepting that due to influenza. In eight of the twenty-two cases it lasted three days or less; and in two-thirds of the entire number it was six days or less. It presents greater difficulties of diagnosis than any of the other forms; in the first place for anatomic reasons. The lesion is usually most marked at the convexity and may be limited to that part of the brain. The diagnosis of a convexity meningitis is proverbially difficult, for many of the most characteristic signs such as opisthotonos, irregularity of pulse and respiration, cranial-nerve involvement and distention of the fontanel, are usually wanting. Again, pneumococcus meningitis has been in my experience seen in younger patients than either cerebrospinal or the tuberculous form. Half of our cases occurred in infants under six months old, and two-thirds were under nine months. It has long been my belief that pneumococcus meningitis, like pneumococcus pericarditis and peritonitis, was the result of a generalized pneumococcus infection occurring much more frequently in very young patients than in those who were older. This has been confirmed by finding the pneumococcus in the heart's blood in every one of seven cases of pneumococcus meningitis in which cultures have been made.

TUBERCULOUS MENINGITIS

I have already said that 70 per cent. of my cases of acute meningitis, apart from the epidemic of cerebrospinal meningitis, were tuberculous. Its great frequency I am sure is not appreciated. During the past four years 8 per cent. of the deaths in the Babies' Hospital have been from this cause. I may have overlooked some cases but I think not many; for autopsies are obtained in this institution in nearly 50 per cent. of the fatal cases, which is a larger proportion than in any other hospital of the City so far as my knowledge goes. Besides, every suspected case receives lumbar puncture and the cerebrospinal fluid is examined both microscopically and by culture. We may safely say that none have been wrongly diagnosticated, for in all but two cases bacilli have been found.

In general practice tuberculous meningitis is certainly very often overlooked or a mistaken diagnosis made. Of thirty successive cases admitted to the hospital, in only three was the diagnosis of tuberculous meningitis previously made and in only three others was it suspected. The most common diagnosis with which the child was admitted was either some gastric disorder or cerebrospinal meningitis.

There are two common misconceptions regarding tuberculous meningitis: the first is that it is a disease of long duration, often lasting two or three months or even longer. I have never seen tuberculous meningitis last over five weeks, and only once have I seen it last five weeks, this in a child of nine years. Of the cases reported in this paper, in infants chiefly, the average duration has been about two and a half weeks after the first definite symptoms of illness appeared. A second error is that tuberculous meningitis usually affects delicate infants, those suffering from malnutrition, often of the marasmus type. The inference is drawn that because a child with symptoms pointing to meningitis was previously in good health, the process could not be tuberculous. It is my experience both in hospital and private practice that the vast majority of these patients have been, previous to their attack, apparently in as good health as any children whom I see. Not that very healthy infants are more prone to tuberculous meningitis than others, but that a tuberculous infection of a young child is very apt to involve the brain early, before there is time for the symptoms which result from a general tuberculosis to be manifest. Some reasons for this will appear later.

Seasonal Prevalence.—That tuberculous meningitis occurs more at one season of the year than at another has not, so far as I am aware, hitherto been noted. For the last two or three years I have been struck with the fact that more patients were admitted during the spring months than at other times and I have had the earlier records of the hospital searched to ascertain the month when patients were admitted.

Chart 1 shows by months the time of admission of 218 patients in the Babies' Hospital service. It will be noted that the curve is at its lowest during the summer and early fall; that there is a slight rise in December and January, but a very sharp rise in the spring months, the highest point being touched in the month of April; the number of cases in the spring months of March, April and May being about twice as great as were seen at any other similar period during the year. A steady fall is noted during the summer until October is reached.

The explanation for this variation is not altogether clear. The most plausible one seems to be that these infants have been infected some time previously and are carrying a latent focus somewhere in the respiratory tract, usually the bronchial glands. Under the influence of acute respira-

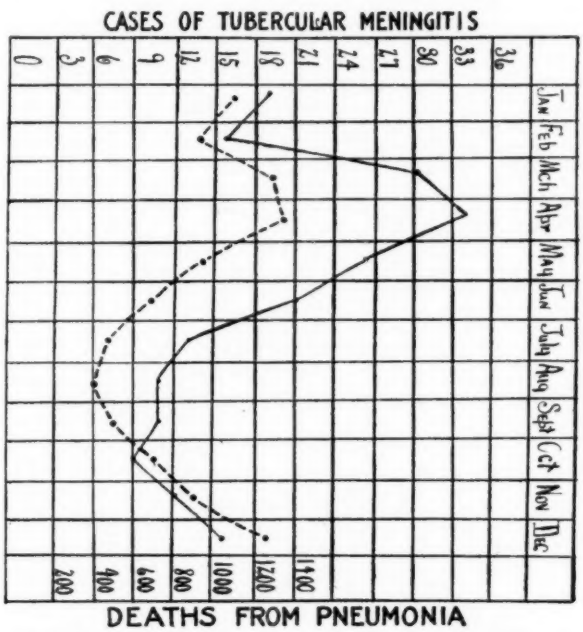

Chart 1. The upper curve represents the seasonal occurrence of 218 cases of tuberculous meningitis; the lower curve represents the deaths from pneumonia in New York City for one year.

tory infections occurring during the winter and spring months, the latent tuberculous disease becomes an active process and a rapidly spreading infection occurs; for in none of these infants is the brain lesion the only one. At autopsy pulmonary lesions are almost invariably found; and miliary tubercles are usually present in many other organs. This indicates that the meningitis in infants is a part of a generalized infection and causes death before the other evidences of the disease are usually manifest. Some of these children showed a few scattered râles in the chest;

and, still more infrequently, evidences of more serious pulmonary disease were present; but the great majority of them showed no pulmonary signs of disease whatever.

An attempt has been made to see in how many cases of tuberculous meningitis bacilli could be found in the sputum. In many it has been difficult to secure any proper sputum for examination. Yet in 116 patients in whom the effort was made, bacilli were found in forty-nine. These cases were taken routine, not selected because of the presence of pulmonary signs or symptoms. It is true that the number of bacilli is seldom large and unless careful and sometimes repeated examinations are made, they are likely to be missed. Yet when present they were found

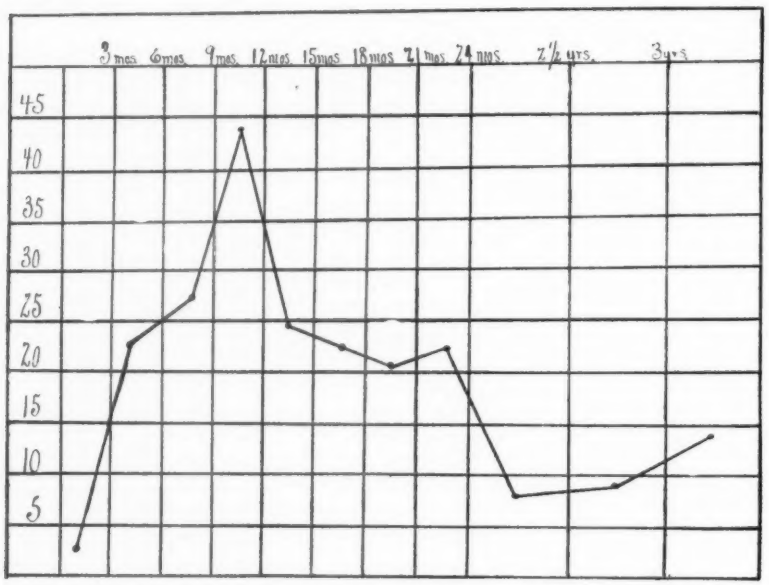

Chart 2. The age incidence in 218 cases of tuberculous meningitis.

at the first examination in three-fourths of the cases, although in one case, not until the sixth examination.

The close association of tuberculous meningitis with inflammations of the respiratory tract is also suggested in the accompanying chart. The lower curve in Chart 1 shows the deaths from pneumonia in New York City for 1909. The similarity of these two curves is certainly striking. I do not think that the tuberculous meningitis in older children would show so close an association with pulmonary disease as is true in infancy.

Age Incidence.—Chart 2 shows the age incidence. Inasmuch as the Babies' Hospital admits children up to three years of age the curve I think may be taken to represent pretty accurately the occurrence of the disease in patients below that age. Only three patients under three

months of age were seen; the greatest number of patients were seen between the ages of nine and twelve months, a rapid decline in the curve being noted after the first year. This is a striking fact, but the reason for it is not very clear. The greater frequency of tuberculous meningitis in children from nine to twelve months of age may be due to the closer exposure of young infants to infected adults than occurs with children who are somewhat older. It is possible also that a closer exposure occurs in winter than in summer and that this may have some bearing on the greater frequency of the disease in the spring months. The incubation period is at present unknown. It seems probable that in most cases it is several weeks at least.

Source and Type of Infection.—It is my experience that nearly all the cases of tuberculous meningitis, the source of whose infection we have been able to trace, have their origin in exposure to adults with pulmonary tuberculosis. A striking confirmation of this is shown in the results of the observations made by Dr. W. H. Park in the Research Laboratory of the Health Department on thirty-two cases in my series in which the type of bacillus was worked out. In thirty it was of the human type; in one it was of the bovine type; in one case both types were present.

The von Pirquet Reaction.—The statement frequently has been made in medical literature that comparatively few infants with tuberculous meningitis respond positively to the von Pirquet test. Systematic observations on this point have been made during the past two years. Of sixty-five cases a positive reaction was obtained in fifty-one; a negative in eleven, and doubtful in three. Of the fourteen cases that were negative or classed as doubtful, four patients were moribund and seven extremely prostrated and with feeble circulation. In the remaining three there was no apparent reason why a reaction should not have been obtained. I regard the skin test, therefore, as of very great diagnostic value, and a negative result, except in the conditions just mentioned, of much diagnostic importance.

I have attached so much importance in recent times to the von Pirquet test and the findings of the examination of the cerebrospinal fluid, that negative results in either of these I have come to regard as very significant. A baby seven months old was admitted with a fairly typical history of tuberculous meningitis: onset with vomiting, slight fever, convulsions developing in three or four days; drowsiness merging into stupor; marked constipation. The prominence of the fontanel was so great that the mother herself had noticed it and, in fact, the "lump on the head" was one of the reasons why the child was brought to the hospital. Lumbar puncture was made and 120 c.c. of perfectly clear fluid removed. It was under very high tension. So confident was I that this was a case of tuberculous meningitis that the search for the bacilli in the cerebropsinal

fluid was continued for several hours, but with negative results. Greatly to my surprise the child did not respond to the von Pirquet test, but what was still more unusual, the child promptly recovered and at the end of a week was discharged to all appearance quite well. It died about one month afterward rather unexpectedly, but without cerebral symptoms, so the visiting nurse learned. I have seen an almost identical picture in another child, in whom recovery was complete and permanent. The explanation of these is rather difficult without assuming the existence of a primary acute serous meningitis, regarding which I have always been rather skeptical.

CONCLUSIONS

Lumbar puncture has placed the diagnosis of meningitis on a new basis. It should be employed in every suspected case. It is only with very rare exceptions that to a skilled observer it gives uncertain results.

Nearly three-fourths of the cases of acute meningitis in young children are tuberculous, except when cerebrospinal meningitis is epidemic.

In tuberculous meningitis bacilli are always present in the cerebrospinal fluid; although difficult to find in the early stages, in the later stages a careful examination should discover them. The von Pirquet test in most cases gives positive results.

In infants and very young children tuberculous meningitis occurs usually as an early manifestation of a general tuberculosis, and generally causes death before the lesions elsewhere are far enough advanced to give definite signs or symptoms. Pulmonary lesions are present in nearly all cases.

Tuberculous meningitis is of human origin. Altogether the most frequent cause is exposure to adults with pulmonary tuberculosis.

The age incidence and the seasonal occurrence are points which are not yet fully explained.

Pneumococcus meningitis usually occurs in younger patients and is associated with pneumonia. Clinically it resembles meningococcus meningitis but usually the course is shorter. It is almost invariably fatal.

Influenza meningitis is infrequent and also resembles the cerebrospinal form. It is almost invariably fatal.

Streptococcus and staphylococcus meningitis are very rare forms in infancy, usually occur in the new-born and are often associated with spina bifida. Under such circumstances they are always fatal. From mastoid disease this form is seldom seen in young children.

Meningococcus meningitis is really the only variety in which at present there may be said to be any hope of recovery. The results in this variety of meningitis have been very greatly improved by the serum treatment.

14 West Fifty-Fifth Street.

THE CONSTANT PRESENCE OF TUBERCLE BACILLI IN THE CEREBROSPINAL FLUID OF TUBERCULOUS MENINGITIS

WITH OBSERVATIONS ON THE CEREBROSPINAL FLUID IN OTHER FORMS OF ACUTE MENINGITIS *

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A systematic effort has been made since March, 1906, in the laboratory of the Babies' Hospital, to determine the presence of tubercle bacilli in the cerebrospinal fluid in cases of tuberculous meningitis. One hundred and thirty-eight patients have been admitted to the wards of the hospital since that time, but fluids for examination were obtained from 137 only. In all but two, tubercle bacilli were demonstrated in the cerebrospinal fluid. The technic which was followed in demonstrating the bacilli has given such satisfactory results that it is herewith given in detail.

TECHNIC

The cerebrospinal fluid is collected in several test tubes, allowing about 20 c.c. to a tube. The last fluid withdrawn after the child has been raised to the sitting posture is considered the most important, as the bacilli are usually found more readily in this. Care must be taken not to shake the tubes. It has been found that a fibrin coagulum, the so-called "film," forms more often in tubes which have not been agitated. The fibrin coagulum is at first very delicate and friable. It forms with greater regularity and becomes firmer in fluids which have been placed in the incubator over night. After ten hours it is usually so firm that the entire film can be removed with a platinum loop. It is then carefully spread with fine needles on a glass slide. This is stained by the carbol-fuchsin Gabbett method. Bacilli were found with comparative ease in every case in which the film formed. In several cases in which the question of immediate diagnosis was extremely important, there was a sufficient coagulum after the fluid had stood three hours to enable one to find the bacilli.

In about 4 per cent. of the fluids examined this coagulum did not form at all. One of the following devices was then used: The sides of the test tubes were scraped with a platinum loop and any material

*From the Laboratory of The Babies' Hospital, New York.

removed, superimposed, drop by drop, over a small area on a glass slide, each drop dried in the air and fixed in the flame before another was added. Or with a fine capillary tube, the sediment from the test tube was superimposed in the same manner. In a few cases the sediment from centrifuged fluid was used. If the fluid drawn early in the disease showed no coagulum and if no bacilli were found, then at the second puncture, before the needle was withdrawn, it was pushed slightly forward so as to touch the anterior surface of the spinal canal, and one or two drops of blood allowed to flow into the last fluid withdrawn. With the addition of the blood a coagulum would often form, when the other tubes of fluid, drawn at the same time, remained clear.

The length of time required to find the tubercle bacilli varied greatly in different cases. Often they were found in a few minutes. If not readily discovered, careful search through the entire film was made. When a moderate number of bacilli were present, a thirty to forty minute search was usually rewarded by the finding of isolated organisms or several in clumps. In no case was a single bacillus considered conclusive. The films from all the tubes sometimes had to be used, and the bacilli were then found after a two- or three-hour search. The average time consumed was about an hour. The amount of fluid removed has averaged 60 c.c. although frequently twice as much has been obtained.

FINDINGS

The cerebrospinal fluid in tuberculous meningitis is usually as clear as distilled water, and often, although not invariably, there are seen floating in it, very small white flecks. In only one case was there a distinct cloudiness. In this the film showed far more polymorphonuclear cells than usual, and also a very large number of tubercle bacilli in each field. Repeated cultures and examinations made in this case, however, revealed the presence of no other organism. In all the other cases the predominating type of cell was the mononuclear, with very few scattered polymorphonuclear cells.

Of the 138 cases of tuberculous meningitis, tubercle bacilli were found in the fluids of 135. Of the remaining three, in one only was an early puncture possible, because the child was removed from the hospital during the first week of illness. No bacilli were found in this fluid, but a guinea-pig was inoculated and eight weeks later showed characteristic lesions of tuberculosis. Another child was brought to the hospital moribund. The diagnosis of tuberculous meningitis was evident from the history obtained from the physician. Only 2 c.c. of clear fluid could be obtained by lumbar puncture, not enough for a satisfactory examination. In the third case no puncture was made, as the child died a few minutes after admission. The diagnosis rested on the clinical symptoms.

Bacilli were therefore missed but once when a satisfactory amount of fluid could be obtained for examination, and that was from a puncture made very early in the disease.

There is little doubt that the bacilli are more numerous late in the disease, yet they were found in the first puncture in 117 cases; in the second in thirteen; and in the third puncture in four cases. Most hospital patients are not admitted until symptoms are tolerably well marked. It is therefore somewhat difficult to say how early in the disease bacilli may regularly be found. On the average, the first puncture was made about ten days before death. The larger amount of fibrin found in the fluid late in the disease, as evidenced by the constant formation of a film, renders the discovery of the bacilli easier at that time. The four cases in which a third puncture was necessary were admitted with symptoms suggesting meningitis. The early puncture showed only an excess of clear fluid, under slightly increased tension, and a few mononuclear cells.

FINDINGS IN OTHER FORMS OF MENINGITIS

Examination of the cerebrospinal fluid was made in twenty-two cases of pneumococcus meningitis. The fluid in twenty of the cases could not have been distinguished macroscopically from turbid fluids in other forms of meningitis. It varied from a slight cloudiness to such a turbidity as to cause a thick deposit of pus in each tube. The cells were chiefly polymorphonuclear; the organisms were plentiful in the smears, and grew readily in cultures.

In contrast to these typical cases, it may be of interest to mention the findings in some other cases, which were quite exceptional. A child with lobar pneumonia showed definite meningeal symptoms. An excess of clear fluid under increased tension was obtained twice by lumbar puncture, and from both fluids the pneumococcus was grown in pure culture. The disease terminated by crisis, the nervous symptoms disappearing with the fall in temperature, the child making a prompt recovery. The case was certainly not one of meningitis.

In twelve other cases of pneumonia with very pronounced nervous symptoms, punctures were made, but in none was the pneumococcus found. In cases of pneumonia with a high temperature, if a puncture was made, the cerebrospinal fluid was usually found to be under increased tension and in excess of the usual amount. This has later been observed to be true in many other diseases in which lumbar puncture has been done on children with nervous symptoms suggesting meningitis, the true diagnosis being made later. In one case, which was proved by autopsy to be one of pneumococcus meningitis, three punctures showed normal fluid in the acute stage. This finding, which was a very remarkable one, sug-

gests that one cannot draw the conclusion that because the cerebrospinal fluid is negative, there is no meningitis present.

The cerebrospinal fluid in the four cases of influenza meningitis all showed great turbidity, the cells were practically all of the polymorphonuclear variety, and the influenza organism was readily cultivated. An examination of a smear from the fresh fluid shows at once that the organism is not the meningococcus, and a culture on blood agar should therefore immediately be made. Cultures on ordinary media would show no growth and one would easily be misled if one relied on them. The organisms are not numerous in the smears, in marked contrast to the great numbers of organisms in cases of pneumococcus meningitis.

In a series of twenty-four meningococcus cases, the fluid from twenty-two showed the usual turbidity, great numbers of polymorphonuclear cells and the presence of the meningococcus in the smears and by culture. In two cases the findings were unusual. One was that of a six months old child admitted in the second week of illness with a history strongly suggesting meningitis. By lumbar puncture 15 c.c. of clear fluid was obtained, which was negative by smear and culture. A very few polymorphonuclear cells were found. The fever and nervous symptoms increased with such severity that a second puncture was made seven days later, and 20 c.c. of slightly turbid fluid obtained, in which the meningococcus was easily demonstrated. From this time the course of the disease was that of a rather mild cerebrospinal meningitis.

An almost identical history was that of a nine months old child, admitted after an illness of four weeks. The symptoms were rather indefinite. The first puncture in this case also showed clear fluid and no organisms of any kind could be found. Two weeks later the fluid was that of a typical cerebrospinal meningitis and the meningococcus was grown from fluids obtained at four subsequent punctures. From a study of these histories the question arises whether there may not be a definite meningeal inflammatory lesion present with, at the same time, a clear cerebrospinal fluid from which no organisms can be cultivated.

In the ten cases of streptococcus meningitis the fluid from each showed great turbidity. There were many polymorphonuclear cells present. The streptococci were present in large numbers and grew readily on ordinary media.

There were three cases in which more than one type of organism was found. In one case tuberculous meningitis occurred six weeks after recovery from a meningococcus meningitis. In another, tubercle bacilli and streptococci were both present during the acute stage. In the third, pneumococci and meningococci were both isolated from the thick, purulent fluid.

OTHER TESTS OF CEREBROSPINAL FLUID

Tests with Fehling's solution were made on 111 fluids to determine the diagnostic value of the presence of a reducing substance. The results were so inconstant that no reliance could be placed on this test in differentiating between tuberculous and other forms of acute meningitis. The results are embodied in the following table:

Form of meningitis	Reduction	No Reduction	Total
Tuberculous	24	26	50
Meningococcus	3	29	32
Pneumococcus	2	2	4
Streptococcus	.	1	1
Normal fluids	23	1	24

These findings suggest that a reduction in normal fluids is the rule, and yet there is reduction in so many cases of tuberculous meningitis that the test is of no value in diagnosis.

The globulin test of Noguchi has been used only recently. It consists of a precipitation of an excess of globulin by means of a solution of butyric acid in normal salt solution, and the addition of a sodium hydrate solution. Seventeen cases of meningitis—eight tuberculous, five meningococcus and four influenza—all gave typical positive reactions. Of twenty-two normal fluids tested, all but two gave a negative reaction. Of the two apparently normal fluids giving a positive test, one was from an acute case of enterocolitis with toxemia and a temperature of 107 F. The cerebrospinal fluid, which was clear, was injected into a guinea-pig and ten weeks later no evidence of tuberculosis or other disease could be found. The other fluid was also from a case of colitis, the autopsy in which showed no meningeal lesion. This test appears to be of great value in differentiating normal from abnormal fluid.

INFLUENZAL MENINGITIS AND ITS EXPERIMENTAL PRODUCTION *

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The extension of the practice of employing lumbar puncture as an aid to the diagnosis of meningitis has had, as one effect, the establishment of the important fact that the influenza bacillus is a not infrequent cause of sero-purulent meningitis. That the influenza bacillus may act as a cause of acute inflammation of the meninges has been known since the publication of Pfuhl's[1] illustrative cases in 1892, but that it acts as a not infrequent cause of that condition we are just beginning to learn. Influenzal meningitis appears to be a very severe and highly fatal form of meningitis and to be exceeded in respect to its fatality only by the pneumococcus and tuberculous forms. It remains, however, for the present, an undecided question whether influenza bacilli may not occur in the cerebrospinal fluid without setting up inflammation, just as pneumococci and some other organisms have been known to do. The frequency with which influenza bacilli occur in the cerebrospinal fluid in all conditions has not yet been determined.

There have come under my observation within the past year eight cases of influenzal meningitis, from which the influenza bacillus was isolated in every case from the fluid removed by lumbar puncture, and the cultures studied in respect to their biologic reactions. All the cases terminated fatally.

TECHNICAL METHODS

The influenza bacillus is a slender rod, somewhat varying in size, staining deeply at the poles, and being Gram-negative. Its invariable and most prominent characteristic is its hemophilic property, next to which pleomorphism is its most striking attribute. It may be considered as conclusively established that a pseudo-influenza bacillus, as distinct from the true influenza bacillus, producing pathologic conditions in human beings, does not exist.

The cultivation of the influenza bacilli dealt with in this paper was made exclusively on agar mixed with rabbits' blood. Petri plates and slanted tubes of the medium are readily prepared by adding a few drops

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* From the laboratories of the Babies' Hospital and of the Rockefeller Institute.

* Read before the joint meeting of the Section on Pediatrics of the New York Academy of Medicine and the Philadelphia Pediatric Society, Dec. 8, 1910.

1. Pfuhl: Berl. klin. Wchnschr., 1892, xxix, 979 and 1009.

of the rabbit's blood to the melted agar, previously cooled to 45 C. I to use rabbits instead of pigeons for securing the blood, because of the greater ease with which considerable quantities of blood can be obtained from the rabbit. It was found that when the blood was mixed with the agar, a better growth of colonies could be secured, and they could be studied more readily. It was preferred to counterstain the Gram preparations of the bacilli with 10 per cent. aqueous safranin, since that stain brought out plainly the poled extremities.

It has been the custom at the Babies' Hospital for the past two winters to take cultures on blood-agar plates from the pharyngeal and bronchial secretions of almost every child admitted during some period of its stay in the hospital. When patients came to autopsy routine cultures on blood-agar were prepared from both lungs and the blood of the heart. In this way we have collected a considerable number of different cultures and strains of the influenza bacillus and numerous data on its occurrence in the body of children during life and after death.

CLINICAL CASES OF INFLUENZAL MENINGITIS

Within a little more than a year, specimens of cerebrospinal fluid from eight cases of influenzal meningitis have come into my hands for study. In some instances, the fluid was sent to the Rockefeller Institute to be examined for *Diplococcus intracellularis* and the influenza bacillus was discovered accidentally. In other cases, the patients were admitted to the Babies' Hospital, where the fluids were examined and in one case an autopsy was performed.

CASE 1.—The turbid fluid obtained by lumbar puncture from this case was sent to the Rockefeller Institute by Dr. Agar who, in association with Dr. Avery, has already published an account of it.[2] Film preparations prepared from the fluid showed a large number of Gram-negative bacilli, some of which were very small, some quite plump and larger. Cocci were absent. Polymorphonuclear leukocytes were present in numbers, a few of which had taken up the bacilli. No growth of the organisms was obtained on plain or serum-agar, but cultivation was successful on blood-agar, on which small, moist translucent colonies developed. These were composed of minute, slim bacilli. There was entire absence of the larger plump forms but the latter, together with some longer, curved bacilli, appeared in the cultures forty-eight to seventy-two hours old. They represented involution forms, since the plates showed the growth to be pure.

CASE 2.—About 3 c.c. of turbid fluid obtained from a child 3 years old was sent to the Rockefeller Institute for examination from the Lebanon Hospital. Flakes of thick pus occurred in the fluid and adhered to the sides of the test tube. Cover-slips showed many polymorphonuclear leukocytes, some of which contained small Gram-negative bacilli. Outside the leukocytes, smaller bacilli were numerous. The bacilli were, for the most part, short, but some moderately long threads occurred. No growth took place on plain or serum-agar, but a characteristic growth was obtained on the blood-agar.

CASE 3.—About 6 c.c. of very turbid cerebrospinal fluid obtained from a child 2 years old was sent to the Rockefeller Institute for examination. Film preparations showed many polymorphonuclear leukocytes and numerous short Gram-

2. Arch. Pediat., 1910, xxvii, 284.

negative, poled, regular bacilli. Rarely were the bacilli found within the leukocytes. The organisms did not grow on plain or serum-agar, but did grow on blood-agar.

CASE 4.—About 50 c.c. of very turbid fluid was obtained from a child about 4 years of age which, on standing, deposited a thick layer of pus. The film preparations showed numerous polymorphonuclear leukocytes and very large numbers of Gram-negative minute, regular, poled bacilli. A very few thread forms occurred. Blood-agar cultures gave a pure growth. A second specimen of the cerebrospinal fluid, more purulent than the first, gave a similar culture in result. The cultures of the influenza bacilli were obtained also from the nasopharynx.

CASE 5.—A child, 6 months old, admitted to the Babies' Hospital. There was a history of convulsions and rigidity for two days, following a period of two weeks of fever and cough. Fifteen c.c. of blood-stained cerebrospinal fluid were withdrawn and the influenza bacillus grown in pure culture. A second lumbar puncture yielded 10 c.c. of a more turbid fluid, from which pus was deposited. The film preparations showed many bacilli, consisting of long and curved, as well as short rods. Cultures on blood-agar were deposited from the second puncture fluid, as well as from the nasopharyngeal and bronchial mucus. No autopsy was permitted, but from the blood withdrawn from the heart one and a half hours after death, a similar bacillus was cultivated.

CASE 6.—A child, 2 years and 10 months of age, admitted to the Babies' Hospital four days after the onset of symptoms of meningitis. Several lumbar punctures were performed during the nine days the child lived, and from 15 to 75 c.c. were withdrawn at each puncture. The fluid originally was turbid, gradually became more so, and finally consisted of thick pus. The influenza bacillus was grown on blood-agar from each specimen of fluid. Death occurred on the thirteenth day of the disease. No autopsy was permitted, but blood obtained from the heart one hour after death yielded growth of the influenza bacillus. The mucus from the nasopharynx and from the bronchi also yielded growths of the bacillus.

CASE 7.—A child of 8 months, admitted to the Babies' Hospital after three weeks of illness. At the time there was swelling of the left elbow joint. Two days after admission symptoms of meningitis appeared. Lumbar puncture yielded 35 c.c. of turbid fluid, from which the influenza bacillus was cultivated. Pus aspirated from the elbow yielded a similar growth. Death occurred three days after the appearance of the meningeal symptoms and the autopsy showed extensive purulent leptomeningitis. The exudate was abundant along the superior longitudinal sinus, over the frontal lobes, the cerebellum, pons and medulla, and in the interpeduncular space. The exudate consisted of thick pus. The lateral ventricles were distended with turbid fluid, and pus covered the choroid plexus. The spinal cord was much less involved apparently, but it could not be examined throughout its length. The suppuration about the left elbow extended to the denuded surface of the humerus, the lower epiphysis of which had separated. The lungs showed the lesions of bronchopneumonia and congestion and a moderate amount of bronchitis and tracheitis. Pure cultures of the influenza bacillus were obtained at autopsy from the pus at the elbow and in the meninges, as well as from the heart's blood. The lungs yielded a growth of influenza bacilli and streptococci.

CASE 8.—A boy of 5 months admitted to the Babies' Hospital in a moribund condition. Lumbar puncture yielded 20 c.c. of very turbid fluid, forming an abundant purulent deposit. Film preparations showed polymorphonuclear leukocytes together with many minute, short and regular bacilli, some of which were in pairs. Very few had been taken up by leukocytes. These bacilli proved to be the bacilli of influenza. Blood removed from the heart by means of a syringe half an hour after death yielded a pure growth of *B. influenzæ*. Mucus secured from the pharynx by means of a swab after death did not show this microorganism.

PROPERTIES OF THE CEREBROSPINAL FLUID

The cerebrospinal fluid in the eight cases was, without exception, cloudy and deposited, on standing, a whitish or yellowish sediment, the supernatant liquid remaining somewhat turbid. In the cases in which the progress of the disease could be followed, it was noted that the fluid became successively more purulent and the sediment of pus heavier. Case 7 yielded, on the last day of life, thick pus.

As was to be expected with fluids of the characters described, they all showed, under the microscope, the presence of polymorphonuclear leukocytes in abundance. The number of influenza bacilli present was usually very large. The bacilli occurred free in the cerebrospinal fluid, as a rule, and there was very slight phagocytosis. The morphology of the bacilli varied greatly. In Case 1 the bacilli were long, curved, and the ends often clubbed, corresponding to the involution forms met with in old cultures. The fluid from this case showed but few of the characteristic small forms. In the fluid from Case 2, the bacilli formed long threads but, nevertheless, typical small forms predominated. The bacilli in the fluid from Case 4 were small and regular and agreed with the typical bacilli as seen in recent cultures. However, not only did small numbers of curved forms also occur, but some long threads as well. We observed no examples corresponding with the very long filaments described by Ritchie.[3]

It is of interest to compare the results described for the eight cases, which have come under my observation, with the statement made by Cohoe[4] that the spinal fluid obtained by lumbar puncture from patients with influenzal meningitis may be quite normal in appearance and that influenza bacilli may be contained in these fluids and be overlooked in film preparations, unless carefully searched for. This statement would seem to stand alone, since all the other statements made in the literature of the subject are to the effect that the fluid obtained by lumbar puncture, once inflammation has been set up by the influenza bacillus, is cloudy. Haedke,[5] indeed, reports a case of an adult, in which the fluid withdrawn one day was clear, and the next day, cloudy. Death occurred twenty-four hours after the second puncture, and the autopsy disclosed an epidural abscess and an early localized leptomeningitis. In this case, we must conclude that the clear fluid was withdrawn before the localized meningitis had developed and that the fluid became turbid as soon as inflammation of the meninges appeared. In another case, reported by Trailescu,[6] the fluid obtained by lumbar puncture is described as transparent, but

3. Ritchie: Jour. Path. and Bacteriol., 1910, xiv, 615.
4. Cohoe: Am. Jour. Med. Sc., 1909, cxxxvii, 74.
5. Haedke: München. med. Wchnschr., 1897, xliv, 806.
6. Trailescu: Ref. in München. med. Wchnschr., 1902, xlix, 118.

the microscopic examination is stated to have shown a large number of polynuclear leukocytes together with small bacilli, some of which were within cells, others without cells. It is evident that this fluid could not have been strictly normal in appearance or that the bacilli were difficult to find. The case described by Cohoe[4] was that of an adult who recovered and the fluid was stated to have been slightly turbid. It is, of course, possible that the influenza bacilli may be present in the cerebrospinal fluid without setting up a meningitis, in which case the fluid would be clear, provided the number of bacilli was not great. Future determinations will have to prove whether, in such a case, the protein content of the fluid is not increased, for which determination the use of Noguchi's butyric acid test, or some other test for protein, will have to be employed.

CULTIVATION AND MORPHOLOGY

An effort was made in connection with each of the fluids to cultivate the bacilli present in them on plain-agar, sheep-serum-agar and blood-agar. No growth was ever obtained on the first two media, but a growth was always obtained on the last one. At later intervals, attempts were made to cultivate the different strains on agar free from hemoglobin, but without success, even after eight months of cultivation on the blood-agar. The pleomorphism of the bacilli is brought out clearly by observing cultures from day to day. After growing for fifteen to twenty-four hours, all the strains showed the usual minute, regular bacilli, among which threads were sometimes present in small numbers. On the second day, the curved forms and longer threads had increased in number and the bacilli in thickness while, after seventy-two hours of growth, the usual bizarre forms were present. The degree, as well as the rapidity, with which pleomorphism occurred was increased by cultivating the bacilli on Bordet's[7] potato-blood-agar. After twenty-four hours on this medium, the cultures showed large, curved, irregularly stained elements. It should be noted that the cultures from Cases 4 and 7, which proved to possess the greatest degree of virulence for rabbits and for monkeys, were made up of bacilli regular in outline and short in form. It was shown that the bacilli from Case 7 were equally virulent, whether obtained from the pus from the elbow joint, the cerebrospinal fluid, or the heart's blood.

ANIMAL EXPERIMENTS

The bacilli were inoculated into mice, guinea-pigs, rabbits and monkeys. Mice proved highly susceptible to small injections into the intraperitoneal cavity, whether of the cerebrospinal fluid or the pure cultures of the bacilli. It was not found possible to increase the virulence appre-

7. Bordet: Ann. de l'Inst. Pasteur, 1906, xx, 731.

ciably by passing the organisms through series of mice, although the average dose was found to be reduced in the ninth passage to about one-half the original fatal dose. The peritoneal cavity of these animals contained little exudate, the spleen was always swollen, and the lungs and kidneys congested. The bacilli could always be recovered in pure culture from the heart's blood, peritoneum, and other organs.

Guinea-pigs, weighing about 200 gm. each, succumbed in twelve to twenty-six hours from injections of from one-half to one culture. The peritoneal fluid of these animals was increased, as much sometimes as 8 c.c. could be withdrawn, and it was always turbid. Polymorphonuclear leukocytes and bacilli were numerous but phagocytosis rarely occurred. The spleen was increased to two to three times its normal size; the kidneys were congested and the lungs showed scattered areas of congestion and inflammation. The bacilli could be obtained in pure culture from the heart's blood and viscera, and from the surface of the pia of the brain and spinal cord. Guinea-pigs sometimes survived three or four days, at which time all the fluid had escaped from the peritoneal cavity and a thick fibrino-purulent exudate covered the liver, spleen, etc.

Rabbits of about 1,200 grams inoculated by injection of one culture, twenty-four hours old, into the ear-vein, succumbed in from fifteen to thirty-six hours. Small hemorrhages existed in the parietal peritoneum and within the serous coat of the intestines and beneath the capsule of the liver, pleura and other organs. The spleen was swollen and soft, the kidneys much congested, while the lungs always showed areas of hemorrhage and of inflammation (pneumonia). The membranes of the brain and cord were normal in appearance. Cultures of the bacilli could be obtained from the heart's blood, viscera, urine, and from the surface of the brain and cord. The bacilli were always present in the lungs, but mingled with other bacteria. The mucous membrane of the upper nasal cavities showed, as a rule, deep congestion, and from its surface large numbers of influenza bacilli were cultivated. Cultures from the nasal secretions were always made before the inoculation of the bacilli and influenza-like organisms were not found in them. This precaution was taken also to exclude the possibility of the presence of the "snuffles" bacillus described by Beck.[8]

The most important of this series of animal experiments are those which were conducted with monkeys. Indeed, we succeeded in producing in two species, namely, *Cercopithecus callitrichus* and *Macacus rhesus,* infection of the meninges, by injecting suspensions of influenza bacilli into the subdural space by means of lumbar puncture. Monkeys do not develop symptoms or the lesions of acute meningitis in all instances after the injection of the cultures. The result depends, chiefly,

8. Beck: Ztschr. f. Hyg., 1893, xv, 363.

on the virulence of the culture employed. When one or two cultures on blood-agar suspended in salt solution are injected in the spinal canal, there is no immediate effect, but the first symptoms appear in from six to twelve hours afterward. From the appearance of the first symptoms, the severity rapidly increases and death occurs in from thirty-six to forty-eight hours or somewhat later.

Lumbar puncture made at different periods showed, first, a turbid fluid containing many polymorphonuclear leukocytes and, later, a more opaque or purulent exudate. Within the fluid were many of the bacilli, usually free, but, in a few instances, within phagocytes. Cultures on blood-agar always yielded a pure growth. The autopsy showed purulent exudate along the superior longitudinal sinus and spreading laterally, a turbid exudate over the cord and base of the brain, and a marked exudate in the region of the cord about the site of inoculation. The smears prepared from various parts of the pia-arachnoid of the brain and cord showed varying numbers of bacilli. Cultures were also positive, including the upper nasal mucosa.

Sections showed a purulent leptomeningitis, both on the surface of the brain and within the sulci, as well as over the spinal cord. The exudate was massed chiefly about the blood-vessels. Innumerable bacilli occurred among the pus-cells, many of which were in a state of fragmentation.

Especial reference should be made to a *rhesus* monkey, although it belongs to a series of experiments on which I expect to report later. This animal survived the subdural inoculation of one culture of the influenza bacillus for twenty-seven days. It had entirely recovered from the meningitis which had been set up, the cerebrospinal fluid had become clear, and the bacilli had disappeared. The autopsy showed an empyema at the base of both lungs, the pus of which contained the influenza bacillus in pure culture. The bacilli were not isolated from the heart's blood, brain or spinal cord.

The results of the inoculation of monkeys into the subdural space of the spinal cord with virulent cultures of the influenza bacillus indicate that an experimental form of influenzal meningitis can be produced, which tends to run a rapidly fatal course, in this respect resembling the clinical disease occurring spontaneously in human beings. There is a further resemblance in the changes which occur in the cerebrospinal fluid and through which it first becomes turbid, and then purulent, and, further, in the relation of the bacilli present in the fluid to the cells. Neither in human beings nor in monkeys has phagocytosis occurred to any great extent. The two reports in the literature which bear especially on our experiments are those of Cantani[9] and Ritchie.[3] Cantani injected

9. Cantani: Ztschr. f. Hyg., 1896, xxiii, 265.

influenza bacilli into the brain in rabbits. He observed that non-lethal doses set up a chronic meningitis and sometimes led to the appearance of pus in the ventricles. The bacilli were present and demonstrable by culture and by film preparation. The microscopic examination showed an acute encephalitis. Ritchie[3] inoculated a *rhesus* monkey with two blood-agar cultures in the lumbar region of the spinal cord and the animal died eighteen hours later. The autopsy showed a beginning meningitis, and in film preparations from the surface of the cord and brain, numerous influenza bacilli were found.

VIRULENCE OF THE STRAINS OF BACILLI

We have had the opportunity of studying a large number of strains of influenza bacilli during the past two years, of which four only were found to be virulent for rabbits. It is, perhaps, significant that of these four virulent cultures, three were derived from the cerebrospinal fluid from cases of influenzal meningitis (Cases 4, 7 and 8), and the fourth from the heart's blood at autopsy in a child succumbing to pneumonia. We have endeavored, in many cases at the Babies' Hospital, to obtain the influenza bacillus from the blood of the heart at autopsy, but unsuccessfully, except in the previous case mentioned, until the cases of influenzal meningitis came under observation. In four cases of this infection (5, 6, 7 and 8), the influenza bacillus was obtained from the blood of the heart. The experience of others conforms to our earlier experience. Thus, Wohlwill,[10] who examined many hundreds of autopsies at the Eppendorfer Krankenhaus with this point in view, never secured the bacillus from the blood. Two of the strains of bacilli, which we found to be virulent for rabbits, were also virulent for monkeys. The other two were not tested on the latter animals. One strain of the bacillus obtained from the meninges was found not to be virulent for rabbits and it also was without pathogenetic effect when inoculated into the spinal canal of a monkey. Generally speaking, therefore, high virulence for human beings would appear to indicate high virulence for rabbits and for monkeys also. But this rule, probably, is not free of exceptions. On the other hand, our experience with many strains of the influenza bacillus isolated from the respiratory tract indicates that, in general, the organism possesses virulence for guinea-pigs and mice. One strain only has come into our hands which was devoid of virulence for these animals. All the strains afforded by the cases of meningitis were virulent for small animals. In order to determine this question of virulence, it is imperative that the animal experiments be made immediately after the isolation of the bacilli, since saprophytic cultivation is quickly followed by loss of

10. Wohlwill: München. med. Wchnschr., 1908, lv, 328.

virulence, the time varying between a few days or weeks and months. Some of our virulent cultures have retained their virulence for rabbits for a period of four months.

SERUM REACTIONS

Agglutination reactions are not satisfactory, and no differentiation of strains is possible by this method.

Opsonins are but slightly more satisfactory. In an immune goat serum, the virulent respiratory strain was phagocyted in as high dilutions as any one of the meningeal strains. Serum from a recovered monkey did not phagocyte the bacilli in dilutions above 1 to 20, and no serum from any human case (respiratory or meningeal) gave any better results.

Complement deviation tests I have found out of the question because of the difficulty of preparing a suitable antigen from these organisms, and since it has not been possible by means of suspensions of washed bacilli or sodium hypochlorite extracts of them to differentiate *Bacillus influenzæ* from the Bordet-Gengou bacillus of pertussis, it seemed hopeless to try to differentiate strains by that method.

Protection experiments were made on mice with immune goat serum. This, when given in sufficiently large doses, left the animal alive whether its homologous culture or a meningeal strain were used.

GENERAL CONSIDERATIONS

It would appear from all the facts given that the influenza bacilli isolated from the cerebrospinal fluid from the cases of meningitis are identical with the bacilli commonly obtained from the respiratory tract, and that the chief difference between the bacilli met with in the two situations is one of virulence. This distinction is not fundamental, since equally virulent bacilli are rarely yielded by infections of the respiratory organs.

Since 1903, the number of cases of meningitis due to the influenza bacillus reported in the literature has been increasing. It is significant that in the cases later reported, the influenza bacilli have been found, for the most part, in pure culture, while at an earlier period, mixed infections were more common. This point is probably explained by the imperfect bacteriologic methods originally employed. The frequent finding of the influenza bacillus in cases of endocarditis, purulent arthritis, empyema, appendicitis, peritonitis, meningitis and otitis, as well as their frequent occurrence in the bronchial and nasopharyngeal secretions in cases of clinical influenza, indicates that this organism, like the pneumococcus, is capable of causing inflammations of the serous and mucous membranes anywhere in the body.

A few words should be added on the probable mode of infection of the meninges with the influenza bacillus. It is a well-known fact that the influenza bacilli occur in the nasopharynx in a high percentage of persons exposed to influenza. The upper respiratory tract would appear to be the most frequent portal of entrance into the body for these organisms and to account for their frequent localization in the middle ear, bronchi and lungs. Whether the meninges are infected directly through the lymphatic connections existing between them and the upper nasal mucosa must, for the present, remain an undecided question. The pathogenicity of the influenza bacillus is too slight for monkeys to make it possible to produce in those animals meningitis by inoculating the nasal mucosa. It is of some significance to have learned that after subdural inoculation of the bacilli, the organisms can be recovered from the upper nasal mucosa, suggesting that they are, in part, excreted there. It must, however, be considered that since they also reach the blood they may be secreted from the blood and not directly from the meninges, or that they are contained in the blood in the peripheral circulation, and that a slight injury of the mucosa, inseparable from the making of the cultures, is responsible for their presence in the tubes. That the inoculated animals excrete the bacilli by the nasal mucosa would appear to be shown by the fact that after intravenous injection of the cultures in rabbits, these organisms are met with in the secretions of the mucosa. Normal rabbits and monkeys do not harbor the influenza bacillus in their nasal passages. The bacilli are also excreted by the kidneys in guinea-pigs and rabbits and pure cultures can be recovered from their organs, and usually from the urine as well. Sections of the kidneys showed large numbers of the bacilli lying in the lumen of the tubules, and some within Bowman's capsules. Sections of the lungs showed the bacilli to be present in the capillary blood-vessels of the alveolar walls and in the alveoli themselves. As bearing on the question previously raised as to whether the influenza bacillus can be present in the meninges without setting up inflammation, it should be stated that the surface of the brain and cord of rabbits and guinea-pigs inoculated intravenously or intraperitoneally with cultures regularly yielded pure growths of bacilli, although no lesions or inflammation are associated with their presence.

The bearing of clinical influenza on the origin of influenzal meningitis in human beings is illustrated by the following cases:

In Adams'[11] case, the child, which later developed meningitis, had been only slightly ill, but cases of well marked grippe had occurred in the household. No pharyngeal cultures are recorded. In Case 4 of my series, a distinct attack of clinical influenza preceded the meningitis by a week, and cultures from the throat were positive on the second day of

11. Adams: Arch. Pediat., 1907, xxiv, 721.

the meningitis. In Cases 5, 6 and 7, the influenza bacilli were present in the nasopharynx and bronchial secretion on the first days of the meningitis. Davis[12] gives a definite history of "cold" in four of his cases. In such instances as Case 7 and the one reported by Slawyk,[13] the meningitis must be looked on simply as the terminal effect in a general blood infection with the influenza bacilli. In Hecht's[14] case, the lung was believed to have been the site of the primary lesion. Fraenkel[15] traces one of his cases to a rhinitis, the other to an otitis. Haedke[5] found influenza bacilli in the pus from the middle ear in his case, and Cohoe[4] believes that a chronic otitis media, together with trauma, was responsible for the meningeal localization in his case. Cohen[16] believes that his cases were infected through the respiratory tract.

The facts that Pfeiffer[17] had found the influenza bacilli only at the seat of the lesion and not in the circulating blood, even in inoculated animals, and that killed cultures gave rise to symptoms similar to those produced by live bacilli, were responsible for the accepted idea that all the symptoms and complications of influenza are due to the toxins of the bacillus and not to the organism itself. This, in turn, gave rise to a widespread skepticism as to the correctness of positive reports on the finding of *B. influenzæ* in the living blood. In Cannon's[18] case, this skepticism was undoubtedly justifiable (1893) and in Letzerisch's[19] (1895) even more so, but Meunier's[20] report (1897) of ten cases of bronchopneumonia in young children, in which the bacilli were found during life in blood obtained from the lung eight times and in that from a vein four times, is convincing. It is worth noting that Meunier called attention to the irregular course and fever in such pneumonias, a fact which Holt[21] has emphasized anew. In 1899, Slawyk[12] published the case of a boy, 9 months old, from whom, during life, the influenza bacillus was grown in pure culture from the cerebrospinal fluid and from the blood of the finger, while at autopsy the bacilli were numerous in sections made from the lungs and were present in pure culture in the pus of an abscess at the left ankle. The interesting points about Slawyk's case are two: the proof that the influenza bacilli are demonstrable in the cerebrospinal fluid during life, and the confirmation by Pfeiffer himself of the bacteriology of the case. With Slawyk's publication, the fact

12. Davis: Proc. Chicago Path. Soc., 1910, viii, 39.
13. Slawyk: Ztschr. f. Hyg., 1899, xxxii, 443.
14. Hecht: Jahrb. f. Kinderh., 1903, lvii, 333.
15. Fraenkel: Ztschr. f. Hyg., 1898, xxvii, 315.
16. Cohen, Ann. de l'Inst. Pasteur, 1909, xxiii, 273.
17. Pfeiffer: Ztschr. f. Hyg., 1893, xiii, 357.
18. Cannon: Virchow's Arch., 1893, cxxxi, 401.
19. Letzerisch: Ztschr. f. klin. Med., 1892, xxi, 274.
20. Meunier: Compt. rend. Soc. de biol., 1897, xxxix, 122.
21. Holt: Jour. Am. Med. Assn., 1910, lv, 1241.

was established that *B. influenzæ* is capable of invading the blood stream and of causing multiple purulent lesions throughout the human body. Before that date about twenty cases of general infection had been reported, in the majority of which the *B. influenzæ* has not been found in pure culture. In four of my cases in which it was possible to make a post-mortem blood culture, the bacilli were found in a pure state within one-half to one and a half hours after death. In three of Davis'[12] seven cases, influenza bacilli were found pure in the heart's-blood at autopsy. Bentz and Frye[22] report a positive blood-culture during life, and Cohen[16] found the bacilli in blood obtained from the tip of the finger before death in two of his cases. In Cohoe's[4] recovered case, the blood remained sterile. The difficulties encountered in making effectual blood-cultures in young children during life are probably responsible, in part, for the absence of data on this point. It would seem, however, that in the majority of the fatal cases of influenzal meningitis a general blood infection occurs.

Cases of purulent leptomeningitis due to the *B. influenzæ* have, from time to time, been reported since 1892, when Pfuhl published three cases, in all of which putrefactive bacilli were very numerous. Of the eleven other cases published by Pfuhl,[23] Ghon[24] accepts only one, and even that was not due to the influenza bacillus in pure culture. In 1897 Haedke reported one adult case, which he believes to have been caused by the *B. influenzæ* alone, but which was contaminated after death by putrefactive organisms. In 1898, Fraenkel[15] published two fatal cases in boys of 10 weeks and 9 months of age, respectively. These are the earliest reported cases in young children. Next came Slawyk's[13] report, the first to place cases of general influenza bacillus infection on a sound bacteriologic basis. In 1900, but one case, that of Meunier[25] was reported, and 1901 marked the report of the first recovery from this disease in a 9-year-old boy, observed by Langer.[26] Trailescu's[6] patient, 6 months of age, died. In 1902, four fatal cases were published, of which one (Ghon[24]) occurred in an adult and did not yield pure cultures, while the others were infants (Ghon, 8 months; Simon,[27] 7 months; Dubois,[28] 4 months). In Ghon's case, influenza bacilli were found in the lungs as well as in the meningeal pus at autopsy. The year 1903 records five cases with two recoveries,

22. Bentz and Frye: Woman's Med. Jour., 1908, xviii, 73.
23. Pfuhl: Deutsch. med. Wchnschr., 1896, xxii, 82; Ztschr. f. Hyg., 1897, xxvi, 112.
24. Ghon: Wien. klin. Wchnschr., 1902, xv, 667.
25. Meunier: Compt. rend. Soc. de biol., 1900, xlii, 5.
26. Langer: Jahrb. f. Kinderh., 1901, liii, 91.
27. Simon: Bull. Soc. Anat. de Paris, 1902, lxxvii, 382.
28. Dubois: Thèse de Paris, 1902.

TABLE 1.—Cases of Influenzal Meningitis with Pure Cultures of B. Influenzæ

No.	Age	Authority	Result	Lumbar Puncture	Autopsy
1	10 weeks.	Fraenkel.	Death.	Not made	*B. influenzæ* from meningeal exudate.
2	9 months.	Fraenkel.	Death.	Not made	*B. influenzæ* from meningeal exudate.
3	9 months.	Slawyk.	Death.	Cloudy fluid; cultures positive. Also from blood of finger.	*B. influenzæ* from meningeal exudate and malleolar abscess.
4	16 months.	Meunier.	Death.	Not made	*B. influenzæ* from meningeal and pleural exudate.
5	9 years.	Langer.	Recovery.	Purulent fluid; cultures positive	
6	6 months.	Trailéscu.	Death.	Transparent, many leukocytes; cultures positive	*B. influenzæ* from meningeal exudate.
7	8 months.	Ghon.	Death.	Cloudy fluid; cultures positive	*B. influenzæ* from lungs with cocci.
8	7 months.	Simon.	Death.	Turbid fluid; cultures positive	No cultures made at autopsy.
9	4 months.	Dubois.	Death.	Turbid fluid; cultures positive	No autopsy.
10	8 months.	Mya.	Death.	Turbid fluid; cultures positive	No cultures made at autopsy.
11	1 year.	Mya.	Death.	Turbid fluid; cultures positive	No cultures made at autopsy.
12	9 months.	Mya.	Recovery.	Purulent fluid; cultures positive	
13	9 months.	Caccia.	Recovery.	Pure cultures from the fluid, and from the pus of an otitis media with a Gram-negative coccus.	
14	1 year.	Mya.	Death.	Turbid fluid; cultures positive	No cultures at autopsy.
15	8 months.	Jündell.	Death.	Purulent fluid; cultures positive	No autopsy.
16	18 months.	Jündell.	Death.	Not made	Smears positive; cultures failed to grow.
17	12 months.	Cagnetto.	Death.	Not made	Cultures pure from meningeal exudate and spinal fluid.
18	13 months.	Cagnetto.	Death.	Not made	
19	11 months.	Bertini.	Death.	Turbid fluid; cultures positive	Autopsy.
20	7 years.	Thomesco and Groceski.	Recovery.	No details given; cultures pure	
21	4 years.	Cattaneo.	Death.	Purulent fluid; cultures pure	
22	10 months.	Douglas.	Death.	Yellowish fluid; many polymorphs; positive cultures.	Cultures from miningeal pus and middle ears.
23	10 months.	Dudgeon and Adams.	Death.	Turbid fluid; cultures positive	At autopsy, pure influenza cultures from hip-joint, pus and spleen.
24	5 years.	Adams.	Death.	Quite turbid; deposit of pus; pure	No autopsy.
25	4 years.	Sprigg.	Death.	Made after death. Cloudy fluid; cultures pure	
26	21 months.	Bentz and Frye.	Death.	Cloudy fluid; cultures pure; blood culture pure	At autopsy, cultures pure from brain pus, with streptococci in blood.
27	4 months.	Cohen.	Death.	Turbid fluid; cultures pure	At autopsy, no cultures made.
28	1 year.	Cohen.	Death.	Turbid fluid; cultures pure, and also from blood of finger.	No autopsy.
29	8 years.	Cohen.	Death.	Slightly turbid fluid; cultures pure; also from blood of finger, pus in wrist-joint and fluid from lung.	No autopsy.
30	Adult.	Cohoe.	Recovery.	Very slightly turbid fluid; cultures positive	
31	9 days.	Davis.	Death.	Not made	At autopsy, pure cultures from meningeal pus and peritoneum.
32	12 days.	Davis.	Death.	Not made	No autopsy.

TABLE 1.—CONTINUED

33	6 months.	Agar and Avery.	Death.	Turbid fluid; cultures positive.....	At autopsy, cultures pure.
34	19 months.	Ritchie.	Death.	Faintly opalescent fluid; second more turbid; cultures positive.	No autopsy.
35	Infant.	Ritchie.	Death.	Turbid fluid; cultures positive.....	No autopsy.
36	13 months.	Davis.	Death.	Turbid fluid; cultures positive.....	At autopsy, cultures from meningeal pus, heart's blood and pericardial fluid.
37	7 months.	Davis.	Death.	Many polymorphs in fluid; cultures positive.....	At autopsy, cultures from meningeal pus and heart's blood.
38	Infant.	Simon and Aine.	Death.	No details given, but cultures reported pure in all...	Not stated.
39	Infant.	Simon and Aine.	Death.	No details given, but cultures reported pure in all...	Not stated.
40	Infant.	Simon and Aine.	Death.	No details given, but cultures reported pure in all...	Not stated.
41	Infant.	Simon and Aine.	Death.	No details given, but cultures reported pure in all...	Not stated.
42	Child.	Simon and Aine.	Death.	No details given, but cultures reported pure in all...	Not stated.
43	3 years.	Wollstein.	Death.	Very turbid fluid; cultures pure.....	No autopsy.
44	2 years.	Wollstein.	Death.	Very turbid fluid; cultures pure.....	No autopsy.
45	3¾ years.	Wollstein.	Death.	Purulent fluid; cultures pure.....	No autopsy.
46	6 months.	Wollstein.	Death.	Turbid fluid; cultures pure.....	No autopsy. Culture from heart pure 1½ hours p. m.
47	2 years.	Wollstein.	Death.	Turbid fluid; cultures pure; later, thick pus.....	No autopsy. Culture from heart pure 1 hour p. m.
48	8 months.	Wollstein.	Death.	Turbid fluid; cultures pure.....	At autopsy, culture pure from meningeal pus, elbow-joint and heart's blood with streptococci in the lungs.
49	5 months.	Wollstein.	Death.	Purulent fluid; cultures pure.....	No autopsy. Heart's-blood cultures pure ½ hour p. m.

TABLE 2.—Cases Due to B. Influenzæ with Other Bacteria

No.	Age	Authority	Result	Lumbar Puncture	Autopsy
1	Adult.	Högerstedt.	Death.	Not made	Contaminating bacteria not named at autopsy; cultures almost pure.
2	Adult.	Pfuhl.	Death.	Turbid fluid; no cultures	At autopsy, cultures mixed with streptococci and pneumococci.
3	Adult.	Haedke.	Death.	Clear; later, turbid; no cultures	At autopsy, cultures mixed with putrefactive bacteria.
4	5 months.	Peucker.	Death.	Not made	At autopsy, cultures mixed with staphylococci.
5	Adult.	Ghon.	Death.	Not made	At autopsy, cultures mixed with streptococci.
6	2 years.	Hecht.	Death.	Purulent fluid; cultures mixed with Gram-negative diplococci.	
7	6 years.	Bertini.	Death.	No made	At autopsy, cultures mixed with pneumococci.
8	1 year.	Davis.	Death.	Not made	At autopsy, cultures mixed with saprophytes.
9	6 months.	Davis.	Death.	Films characteristic; turbid fluid; cultures failed to grow.	At autopsy, cultures mixed with streptococci.

TABLE 3.—Doubtful Cases

No.	Age	Authority	Result	Lumbar Puncture	Autopsy
1	Adult.	Testevin.	Death.	Fluid with much pus	At autopsy (of spine only), diplo-bacilli of influenza grew on serum agar.
2	3 years.	Nuttall and Hunter.	Death.	Fluid clear; ill two months; cultures of meningococci, and, in smears, bacilli which authors are "inclined to regard" as influenza.	
3	4 months.	Nuttall and Hunter.	Death.	Fluid clear; ill five weeks; cultures of meningococci and, in smears, bacilli which authors are "inclined to regard" as influenza.	
4	1 year.	Nuttall and Hunter.	Death.		
5		Morosow.	Death.	No details given	*B. influenzæ* alone, but no details given.
6	11 months.	Carles.	Death.	Very turbid fluid; smears positive; no cultures.	No autopsy.
7	5 months.	Ritchie.	Death.	Slightly turbid fluid; smears positive; streptothrix grew, but only in one generation.	No autopsy.
8	6 months.	Davis.	Death.	Turbid fluid; films characteristic; cultures not studied.	No autopsy.

both in babies 9 months of age, observed by Caccia[29] and by Mya,[30] the latter publishing three other cases. In the following year, Jündell[31] and Cagnetto[32] each reported two pure cases and Bertini[33] one, all in children between the ages of 8 and 18 months. In 1904 also, a fourth recovered case, in a boy 7 years old, came under the observation of Thomesco and Gracoski.[34] Cattaneo[35] in 1905 reports a fatal case in a 4-year-old boy. During 1907, cases were reported by Douglas[36] (10 months); Dudgeon and Adams[37] (10 months); Adams[11] (5 years); Sprigg[38] (4 years); and Carles[39] (11 months), but in the last case no cultures are recorded, only smears from the abundant fibrino-purulent deposit of the lumbar puncture fluid. Only one case appeared in 1908, reported by Bentz and Frye.[22] In 1909 Cohoe[4] placed on record a recovery in an adult, and Davis,[40] the two youngest patients known, twins aged 9 and 12 days, respectively. Cohen's[16] patients were 4, 8 and 12 months old, but he chooses to look on the bacillus isolated from his cases as distinct from the *B. influenzæ* because of its greater virulence and the difference in its serum reactions when compared with a strain obtained from Pfeiffer. During 1910, Davis[12] reported five additional fatal cases, in infants from 6 to 13 months of age, two being pure. Agar's publication records Case 1 of this paper. Ritchie's[3] description of the "influenza-like" bacillus found in his three cases shows that very many long filaments were present, even in young cultures. The fact that after some months of cultivation on blood-agar the bacillus grew on ordinary agar, on which subculturing was possible for some weeks, would seem to take it out of the class of influenza bacilli. Simon and Aine[41] tell of five cases, four of them in infants. Cases of meningitis, in which influenza bacilli were found in addition to other organisms have been reported by Högerstedt[42] in an adult, Peucker[43] in a 5-months-old baby, Hecht[14] in a child of 2 years, and Bertini[33] in a 6-year-old boy. One of Davis'[12] cases was contaminated by saprophytes, and in another streptococci were present with the influenza bacilli. Nuttall and Hunter,[44] while studying the meningo-

29. Caccia: Ref'd to in Centralb. f. Bakteriol., 1904, xxxv, 106.
30. Mya: Gaz. d. Osp., 1903, xxiv, 268; Riv. clin. Pediat., 1903, xxiii, 465.
31. Jündell: Jahrb. f. Kinderh., 1904, lix, 777.
32. Cagnetto: Cited by Ritchie, Jour. Path. and Bacteriol., 1910, xiv, 615.
33. Bertini: Riv. clin. Pediat., 1904, ii, 673.
34. Thomesco and Gracoski: Rév. neurol., 1905, xiii, 44.
35. Cattaneo: Baumgarten's Jahresb., 1905, xxi, 289.
36. Douglas: Lancet, London, 1907, i, 86.
37. Dudgeon and Adams: Lancet, London, 1907, ii, 684.
38. Sprigg: Am. Jour. Obst., 1907, lvi, 467.
39. Carles: Jour. de med. de Bordeaux, 1907, xxxvii, 106.
40. Davis: Arch. Int. Med., 1909, iv, 323.
41. Simon and Aine: Semaine Méd., 1910, xxx, 513.
42. Högerstedt: St. Petersb. med. Wchnschr., 1895, xii, 123.
43. Peucker: Prag. med. Wchnschr., 1901, xxvi, 153.
44. Nuttall and Hunter: Lancet, London, 1901, i, 1524.

coccus, came on three cases of meningitis in a late stage, in which the clear cerebrospinal fluid contained the diplococci and also bacilli which, from their morphology and staining, they were inclined to regard as influenza bacilli. It is obvious that such cases cannot be accepted without cultural isolation of the bacilli. Morosow's case[45] is given so meagerly that it is difficult to judge of its authenticity. Testevin[46] made a lumbar puncture in an adult case of meningitis and spinal caries, obtaining purulent fluid with an "infected odor." A partial autopsy only was performed, and from the meningeal pus the "diplobacilli of grippe" grew on serum-agar, making this case more than doubtful. All the reported cases are tabulated below.

The great preponderance of cases of influenzal meningitis among young infants and its very high mortality are very striking, as is the opportunity which lumbar puncture gives for early and correct differential diagnosis in this disease. Thus, since Slawyk's positive case in 1899, there have been forty-four cases of pure influenzal meningitis reported, and in thirty-three of these the diagnosis was made from cultures of the cerebrospinal fluid before death. In all there are forty-nine cases of pure and nine cases of mixed influenzal meningitis on record, of which only five were adult subjects, and twenty-eight were under 1 year of age. Five recoveries occurred, all among the pure cases; one patient was an adult, one was 9 years old, another 7 years, and two were 9 months of age.

45. Morosow: St. Petersb. med. Wchnschr., 1904, xxi, No. 6, 40.
46. Testevin: Dauphiné Méd., 1897, xxi, 49.

AMAUROTIC FAMILY IDIOCY *

ISAAC A. ABT, M.D.
CHICAGO

During the year a case of amaurotic family idiocy has come under my observation in my service at the Michael Reese Hospital, Chicago. I was enabled to study the case clinically and also was fortunate enough to secure a complete autopsy. Notwithstanding the fact that numerous cases have been reported by American and European writers, the case is thought to be of sufficient interest to warrant publication.

B. Sachs[1] was the first to use the designation "amaurotic family idiocy," applied to an interesting family disease occurring in infancy, characterized by an entire lack of mental development, by a progressive weakness of all the muscles of the body, and by rapidly developing blindness, associated with typical changes in the macula lutea. The disease is, according to Sachs, generally fatal, the patients dying, as a rule, in a condition of complete marasmus before the end of the second year of life.

REPORT OF CASE

History.—The patient was a male child, 18 months old, born of Jewish parents, and was admitted on Sept. 18, 1909. The birth was uneventful; no forceps were used, and the delivery was easy. The child weighed 10 pounds at birth. The eruption of the teeth came late, beginning at the tenth month. The child progressed normally up to the eighth month of life. Until 1 year old the baby had mother's milk; after that, cow's milk, soup, potatoes, and almost everything. This diet seemed to agree with the baby, and he increased in weight.

History of Illness.—At about 8 months of age, the child began to show signs of listlessness. He moved his limbs very little, the movements being aimless. Paralysis gradually developed, up to the time of examination. The mother stated that the child saw little, or not at all. At the time of examination he could not sit up or move his legs. He could move his hands only a little. For the past ten days he had had difficulty in swallowing. The eyeballs did not act in unison; they rolled from side to side, and also moved outward and upward. This motion was almost constant. Loud sounds, such as slamming of a door, or slight noises, threw him into convulsions, which lasted for several seconds. The appetite was normal; digestion good; bowels normal. For the past two weeks the child had cried more than usual; appeared to be losing in weight. He had had for the past six months, at varying intervals, choking spells. He had suffered from none of the infectious diseases. The only acute illness was a gastro-enteritis two months previous, not severe in character. It lasted about a week.

Family History.—The first child died, in exactly the same condition from which our patient is suffering, at 18 months of age. The second child was 4 years

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* Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-first Annual Session, held at St. Louis, June, 1910.

1. Osler's Medicine, 1910, p. 868.

old and well. The patient was the third child. The mother and father were well, except that father had attacks of asthma. The grandparents' history was negative.

Physical Examination.—General appearance was that of a large child, with a prominent head. Saliva drooled from the mouth. The expression was vacant. The eyes rolled in all directions.

Head: The scalp was negative. Dimensions of head were somewhat larger than normal; the sutures and the fontanels were closed.

Eyes: The pupils were equal, reacted sluggishly to light, and showed a nystagmus, but also an outward and upward movement, which has already been referred to.

The examination of ears, mouth and pharynx, neck, chest, heart and lungs was negative.

Abdomen: Liver was normal in size and position. Spleen was palpable; otherwise negative.

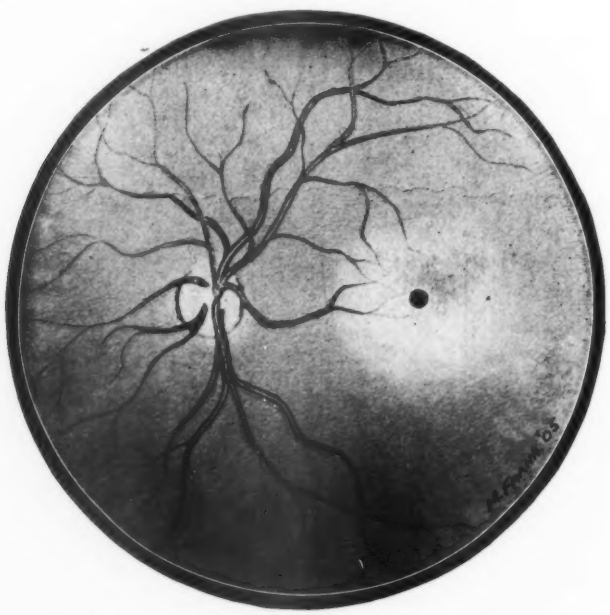

Fig. 1.—Ophthalmoscopic picture of eye ground in a case of amaurotic family idiocy.

Extremities: Arms appeared to be spastic, with a distinct wrist-drop and an outward rotation of the forearms was noted. The arms occasionally showed a flaccid paresis. The spastic and flaccid conditions seemed to alternate. The legs also showed a spastic paralysis and were in the extended position, with a typical foot-drop.

Reflexes: Eyes reacted to light sluggishly. Abdominal reflexes were slow. Knee reflexes were decreased. Babinski sign was present on right foot, but not on left.

Sensations: Tactile and pain sensations seemed to be exaggerated in legs, but not in arms.

Genitals: Right testicle was only partially descended.

Ophthalmoscopic Examination: Dr. Mortimer Frank reported the pathognomonic condition in retina, which was as follows: "About the macula lutea (Fig. 1) is a nebulous area, grayish-white in color, slightly raised above the surface of the

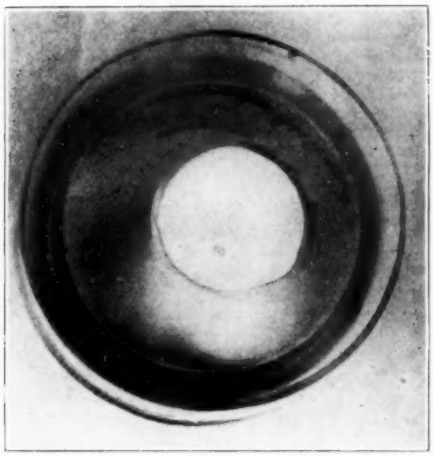

Fig. 2.—Section of posterior half of the eye showing the region about the macula.

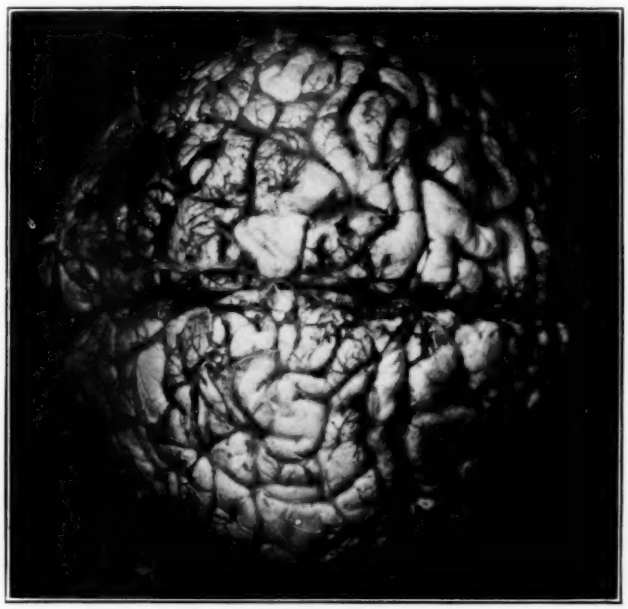

Fig. 3.—Convex surface of brain, case of amaurotic family idiocy. No gross lesion.

retina, and about two to three times the size of the optic disc. The patch is oval in shape, with the major axis horizontal. In the center, coinciding with the fovea centralis, but larger, is a dark red, or cherry-colored spot, clear-cut in outline."

Two spinal punctures were made. The fluid was more than normal in amount; it exuded under high pressure, but was negative as to its microscopic and chemical findings.

The blood, feces and urine were negative.

Course of Disease.—The child lived for twenty-one days after admission. Temperature and pulse were practically normal throughout the disease, with the exception of last few days of life, when the child's temperature rose as high as 106 F.; pulse rapid, running up to 160. Abdominal reflexes appeared to be absent on some days, though on other days they were highly exaggerated. The same was noted of knee reflexes. Babinski sign was present on both sides at

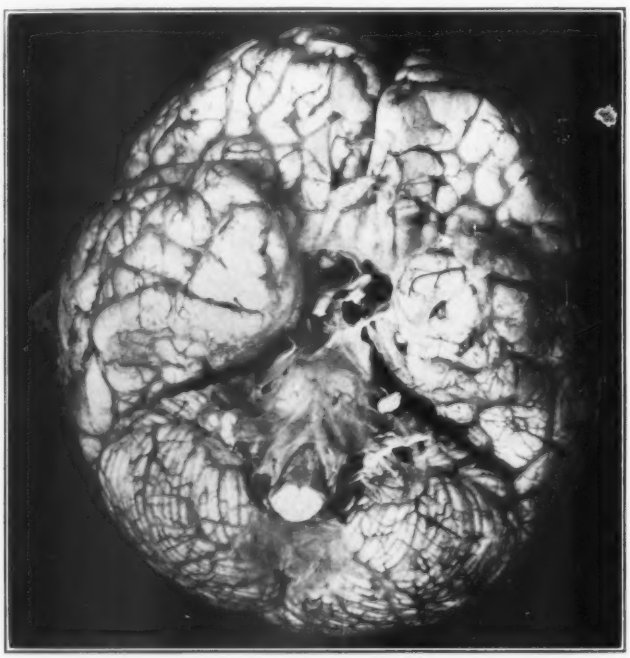

Fig. 4.—Basal surface of brain, case of amaurotic family idiocy. No gross lesion.

times, and occasionally entirely absent. The arms occasionally showed a catatonic state. Clonic convulsions were noted quite frequently, especially when slight noises were made. Choking spells occurred while the child was being fed. Drooling of saliva was almost constant. The child could not support the head. During the last few days of the disease the nystagmus ceased, but a constant outward and upward movement of eyeballs was noted and all the reflexes were exaggerated.

Summary of Clinical Symptoms and Physical Findings

1. Death of two children from this disease in the same family, the patient being the second.
2. Insidious onset, inability to support the head, gradual development of muscular weakness, going on to alternating flaccid and spastic paralysis.
3. Gradual development of blindness.

4. Pathognomonic sign in the macula lutea (cherry spot).
5. Constant and irregular nystagmus.
6. Alternating absence and presence of reflexes.
7. Hyperacusis (increased sensitiveness to sounds), throwing the child into convulsions.

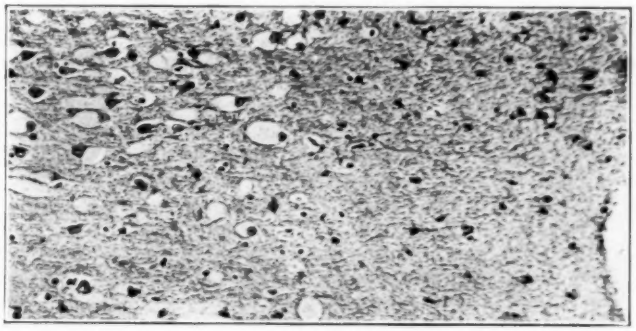

Fig. 5.—Cerebral cortex, parietal area, showing absence of external polymorphous cell layer.

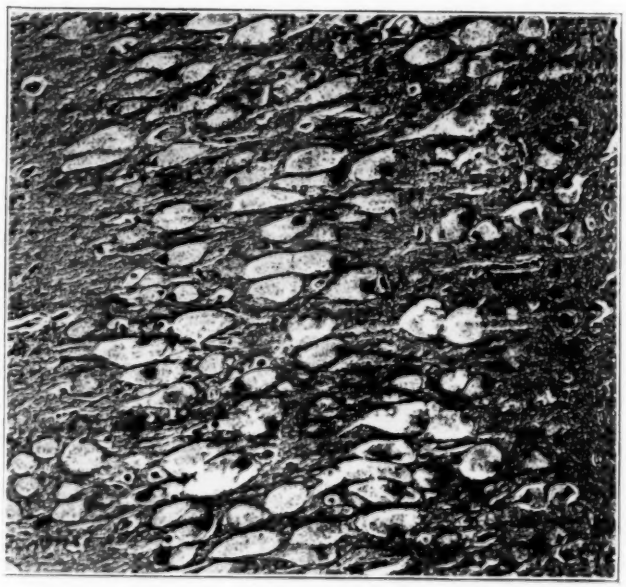

Fig. 6.—Cells in cortical region of hippocampus major. Loss of tigroid substance; eccentrically placed nucleus.

8. Impaired deglutition and choking spells.
9. Digestion normal.
10. Constant drooling of saliva.
11. Last stage of the disease, characterized by loss in fat and weight and marked asthenia.

Pathologic Report on Eyes.—The pathologic examination of the eyes was made by Dr. Mortimer Frank, whose report follows: The specimens were fixed in formaldehyd solution, and cut in an anterior and posterior half, so as to show the area surrounding the macula. The globes before cutting measured 18 mm. from side to side, 17 mm. from before backward, and 17 mm. from above downward. Except for slight corneal abrasions, nothing unusual was found in the anterior halves. The posterior halves presented in the region of the macula a grayish zone, 2 mm. by 1 mm., somewhat elliptical in shape, with the ends pointed, in the center of which was a dark-brown depression about the size of a pin-point, corresponding to the fovea centralis. This area corresponding to the striking ophthalmoscopic picture seen in the living eye. The disks were almost white, with central arteries crossing them. One of the halves was mounted in glycerin-formaldehyd jelly and the other sectioned serially (Fig. 2). A distinct hole, as described by Parsons, was seen, but no edema. Briefly, the changes in the eye

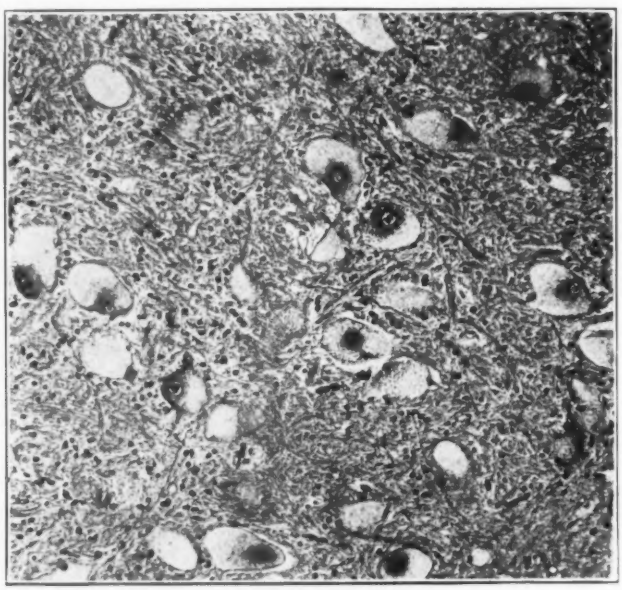

Fig. 7.—Cells of Clark's column. Tigrolysis in some cells; complete loss of tigroid substance in other cells.

were of a degenerative type, affecting chiefly the ganglion cells of the retina, but in a greater degree those in the macula. The optic nerve likewise showed the same degenerative changes.

General Pathologic Report.—The brain and cord were referred by Dr. James W. Jobling, pathologist of Michael Reese Hospital, to Dr. M. G. Schlapp, instructor in neuro-pathology at Cornell University Medical College, who has very kindly furnished the pathologic report. The photographs were taken by Dr. Jaques.

A striking feature about the lesion found in amaurotic family idiocy is the fact that all the nerve cells in the cerebrospinal nervous system are involved. The most distinctive changes in this case are those found in the cerebral cortex (Fig. 5) affecting equally the different areas, but the

Fig. 8.—Section showing cells in anterior horn of spinal column (Bielschowsky's stain). Destruction of intracellular fibrils. The peripheral fibrils still existing and continuing into the dendrites.

Fig. 9.—Cerebellar cortex; granule cells decreased in numbers.

same changes are also to be seen in the cord, especially involving the cells of Clark's column (Fig. 7).

It is impossible to differentiate the several layers of the cerebral cortex, partly on account of the disappearance of many cells, and partly because of the changed appearance of the cells remaining (Fig. 6). The cells of this region, regardless of variety, show a marked swelling of the cell body, almost entire loss of the tigroid substance, and a nucleus which occupies an eccentric position. The disappearance of the tigroid substance seems to have taken place first at the periphery of the cell, and then progressed toward the nucleus. In quite a number the only tigroid substance remaining is in the form of a mantle surrounding the nucleus,

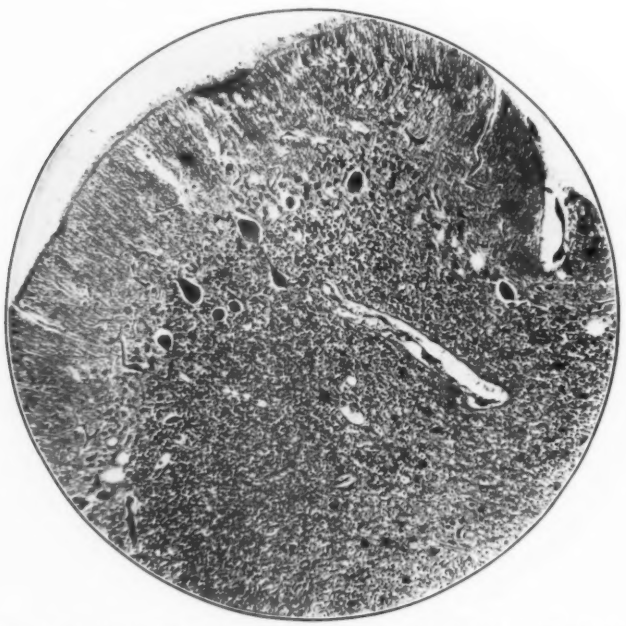

Fig. 10.—Cerebellar cortex (hematoxylin and acid rubin). Nuclei of Purkinje cells retain central position. Tigroid substance beginning to disappear, but found around nuclei.

and in the larger portion of these cells the nucleus is apical in its relation to the cell body, and the tigroid substance, when present, extends into the adjoining dendrites, which also appear swollen. This loss of tigroid substance is confined wholly to the cell body; there does not appear to be any diminution in the dendrites. The marked swelling of the cells, with the loss of tigroid substance, causes the cells to stand out distinctly as light areas, and to assume a balloon appearance. In some cells the nuclei do not present round, well-formed bodies, but are broken up into small fragments, resembling the chromatin substance of the nucleoli. Distinct vacuoles are present in the periphery of some of the cells.

By Bielschowsky's fibril stain it is apparent (Fig. 8) that the intracellular fibrils are being destroyed, and that the fibrils lying at the periphery of the cell body are much better preserved, as are also the continuation of these peripheral fibrils into the dendrites. Excepting for the swollen condition of the dendrites, this stain also brings out the fact that the abnormal changes are confined almost wholly to the cells, the cell processes appearing practically normal.

The changes are least marked in the cerebellum (Figs. 9 and 10) and in the postspinal ganglia. In the cerebellum the layer of granule cells is present, but the number of these cells seems to be diminished. The Purkinje cells show some change, but they are not as marked as are the

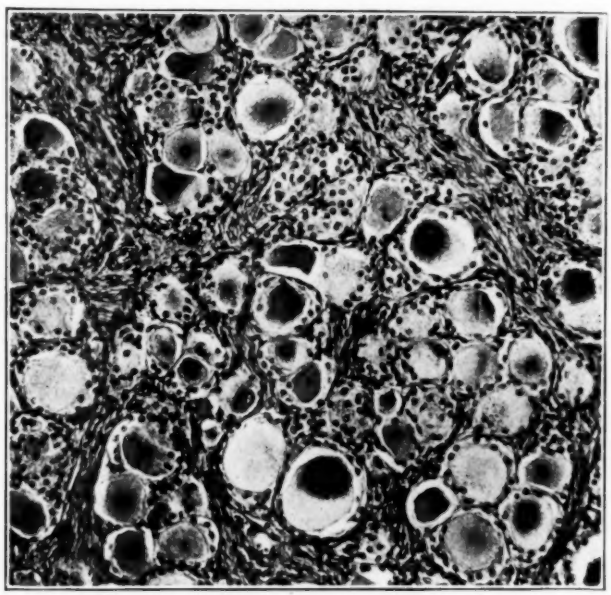

Fig. 11.—Spinal ganglion. Disappearance of tigroid substance. Around nucleus tigroid substance left.

changes in the cerebral cells or nerve cells in other parts of the central nervous system. The nuclei in the majority of these cells retain their central position and stain intensely with hematoxylin. The tigroid substance is beginning to disappear at the periphery of the cells, but is still found around the nuclei.

The nerve cells of the cord (Figs. 11 and 12) show practically the same changes, though to a somewhat less degree, as those already described as occurring in the cells of the brain. They are markedly swollen, and the tigroid substance and intracellular fibrils have in most instances almost entirely disappeared.

We have, therefore, the following marked changes in the cell, recognized by Nissl: hematoxylin, eosin, Van Giesen, and other cell stains:

1. Swollen condition of cell body.

2. Complete or partial loss of tigroid substance. If any tigroid granules are present, they are to be found around the nucleus.

3. Eccentric position of nucleus with various abnormal appearances; irregular outlines; some nuclei intensely stained with hematoxylin, others not; disintegration of nucleolus.

4. Pericellular lymph-spaces much distended.

5. In advanced stages of degeneration a complete disintegration of remaining substance of cell body.

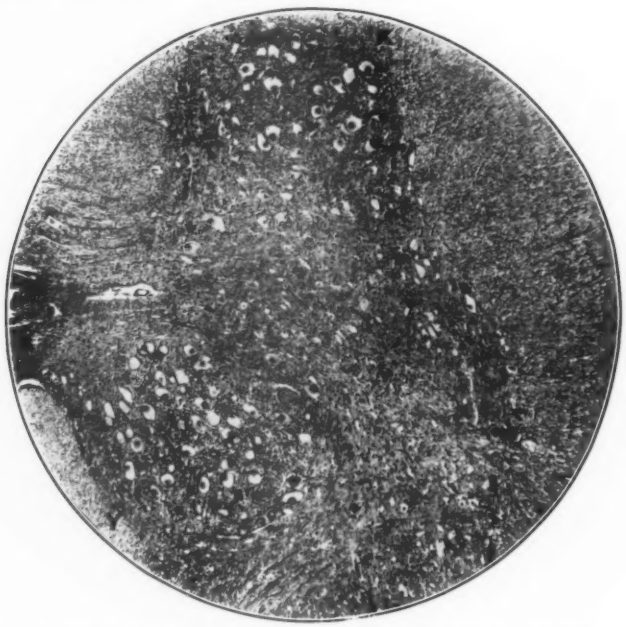

Fig. 12.—Anterior horn (x) of spinal cord and Clark's column (y). Cells swollen. Tigroid substance and intracellular fibers disappear.

CLASSIFICATION

Two forms of amaurotic family idiocy have been differentiated:[2]

1. *Infantile Form.*—The course, as has been frequently described, is characterized by the occurrence of the disease some time during the third or fourth month of life, though the children are born healthy and remain normal until overtaken. Syphilis and other constitutional diseases of the parents are absent. As a rule, several children in the same family are affected. Many of the children come from families having neuropathic

2. Vogt: Arch. f. Kinderh., li, 1.

or psychopathic taint, and at the same time it may be said that the majority of cases occur in Jewish children. According to the statistics of Heverock,[3] who collected reports of eighty-six cases, sixty-one occurred among Jewish children, seven among Christian children, and in seventeen the race and religion were not noted.

The onset of the disease is usually gradual and only after days or weeks of ill-defined symptoms is the disease recognized. First of all, the patients seem to grow less lively; they show lassitude; manifest little or no interest in their surroundings, and desire to sleep. It is also noted that about this time the children do not follow objects with their eyes. Later on, when the physician is called, he suspects that the child is blind or has a seriously defective vision, and the ophthalmoscopic examination shows a light macula with a red punctiform center, and with atrophy of the optic nerve. The changes in the macula precede the pupillary changes. If the child is seen early and is not blind, he soon becomes so. Nystagmus and deviation of the eyes is a frequent occurrence. Hyperacusis, deafness and loss of smell sense are frequently present. The pupils are, as a rule, asymmetrical, and only rarely do they fail to react. Increased salivary secretion with profuse discharge and wide open mouth are frequently reported. The reflexes, particularly the patellar, may be increased, or absent, or unchanged. Frequently the head cannot be held erect and falls on the breast. As the disease progresses, pronounced weakness of the extremities occurs, the child lies motionless, the musculature is relaxed and naturally loss of weight occurs.

Little by little a general paralysis sets in, which is most often flaccid, though occasionally spastic. Later on rigidity of the extremities occurs. Mentally, the children deteriorate and eventually show no reaction. They lose more and more in weight and the disease terminates in marasmus.

2. *Juvenile Form.*—A juvenile form is also described. Clinical observations would indicate that the disease described by Sachs and Fay may occur in juvenile age. Cases of this kind have been described by Higier and Freud and more detailed descriptions by Spielmeyer and H. Vogt.

While Sachs does not deny the close resemblance between these two forms of the disease, he does not consider them identical. The juvenile form, although associated with blindness, does not show the macular changes which are pathognomonic in the infantile form.

100 State Street.

3. Heverock: Neurol. Centralbl., 1904, p. 948.

ATYPICAL SCARLET FEVER*

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Among the diseases of children which we are called on to treat there is none other which may present itself in such peculiar and unusual ways as scarlet fever. This, together with the fact that we have no positive means of proving our case, either clinically or bacteriologically, renders scarlet fever a disease difficult and in some instances impossible of diagnosis.

Thus we see cases of evident scarlet fever showing the typical rash, throat, glands and temperature reaction, and yet the child never desquamates. Is desquamation necessary? A boy 4 years old became ill with what I diagnosed and considered a typical moderately severe scarlet fever. We kept up quarantine for seven weeks, watching for the desquamation which never came in spite of a very intense rash, and which did not appear later.

During a visitation of scarlet fever to a family, four children were attacked. Dr. S. Finley Bell had treated the two other members of the family at Englewood, a suburb of New York; a trained nurse caring for the children contracted the disease and died. Later a girl 6 years old died with the disease. At one of my visits to one of the children who had been sent to New York City and later developed the disease, a member of the family called my attention to the arms of the laundress, which were slightly reddened. It was Monday morning and she was washing. There was no temperature, a normal throat, no rash elsewhere and the girl felt well and was annoyed that she should be disturbed with her work. The redness of the arms disappeared after the completion of the washing and nothing more was thought of the woman until she was found to be desquamating profusely on the hands and feet with slight desquamation over the body generally. She was visited by an expert from the health department and sent to the Willard Parker Hospital where she required two weeks to complete the desquamation. Here was a case in which a most careful search failed to reveal anything approaching conclusive evidence of scarlet fever and yet the woman had the disease at the time.

The father of two of my young patients came into my office and asked me to look at his hands which were desquamating freely, as were also his feet. He said his wife was in the same condition and wanted to know if they had scarlet fever. Two weeks previously they had both had an itching of the skin which they had ascribed to some dietetic error. The

* Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-first Annual Session, held at St. Louis, June, 1910.

mother was seen and was desquamating. I have seen hundreds of children desquamate with scarlet fever and this desquamating was in all respects similar. We isolated the two children who had previously been in daily contact with them and neither became ill, and no other case could be traced to the couple.

A boy 14 years old became ill with tonsillitis and an indefinite rash which was diagnosed as urticaria. After two days the rash had disappeared. The boy recovered from the illness, mixed with other members of the family, which consisted of the father and mother and three other children, two younger than the boy. Not one of them contracted scarlet fever. The boy circulated among his fellows. To my dismay, after three weeks from the beginning of the illness desquamation began on the feet and hands. The desquamation was very free, requiring about three weeks to complete. Did this boy have scarlet fever?

A girl 3 years of age developed a typical scarlet fever rash without temperature and with a normal throat. The rash was characteristic and, since a younger child was in the house, a vigorous quarantine was established. The rash subsided and the skin was clear in five days. At the end of the second week, a very general desquamation of the entire body appeared including the palms of the hands and the soles of the feet. The desquamation was slow, requiring nearly three weeks for completion.

A boy 2 years of age developed a rash somewhat resembling German measles. He had a congested throat and fever. There were other cases of scarlet fever in the apartment. This boy had been exposed and there were other children in the family. An expert from the health department diagnosed the case as German measles and dismissed it. I was not satisfied with the diagnosis and kept the child in quarantine because of the angina in association with a nondescript rash. In three weeks from the onset desquamation began and ran the usual course.

A boy 18 months old, an inmate of a New York institution for children, was noticed, when he was stripped for weighing, to have a typical scarlet fever eruption over the outer left thigh. There was no eruption elsewhere at any time. I was called and confirmed the nurse's diagnosis as to the nature of the rash. The boy had a temperature of 102 F. at the time. He was one of an epidemic of 109 cases. He was very slightly ill. The rash faded rapidly and, of all the 109 cases, he probably desquamated the most freely, the epidermis coming off in large masses.

A girl 5 years of age developed scarlet fever; the attack was moderately severe. Everything occurred on time, the desquamation being completed at the end of the fifth week. Two weeks later the child went to the sea-shore and while walking barefooted on the sand a trained nurse noticed that she was desquamating on the feet. This was reported to the hotel office. The child returned home and went through a second desqua-

mation, requiring about twenty days. One other case of second desquamation has come under my observation.

I was called by Dr. Rodman of New York City to see a boy 6 years of age, ill with scarlet fever. The child was desperately ill, a typical severe case with rash, angina, adenitis, high temperature and prostration. The child died a few days later. On getting the history I was told by the physician that this was the second attack, the patient having recovered from a previous attack three months before, and that there was no doubt as to the previous illness. The mother, an intelligent woman, described in detail the character and duration of the desquamation, substantiating the physician's opinion.

Every year we see cases of acute nephritis following undiagnosed scarlet fever. Usually the rash is very slight, not characteristic and thought to be indigestion, the child being ill but a day or two if at all.

I might recite many other instances of unusual manifestations of the disease under consideration. Enough has been said to bear out the opening statement that scarlet fever is a disease which may manifest itself in peculiar and unusual ways.

A fairly large experience covering hospital and private work for twenty-two years, has led me to believe:

1. In many cases, scarlet fever is never recognized.

2. Scarlet fever is a disease of direct infection; it is rarely carried by a second person or object.

3. The most contagious period is early in the disease during the period of angina, rash, and temperature.

4. The dangers of transmitting the disease during the desquamation period is much exaggerated.

5. Wrongly diagnosed and unsuspected cases are the great transmitters of the disease.

6. During a scarlet fever epidemic, every suspect must be quarantined until he gives reasonable proof of innocence.

7. The most constant symptom is the angina, a deep general congestion of the fauces; but this may fail.

8. In its symptomatology scarlet fever is the most inconstant of the exanthemata.

9. In its severity there are the widest possibilities. I have seen children die in thirty-six hours from the onset, and I have had cases escape my recognition when I was looking for them.

10. It is a disease in which some definite diagnostic sign is greatly to be desired.

132 West Eighty-first Street.

PROGRESS IN PEDIATRICS

ANATOMY AND PHYSIOLOGY

Contributions to the Study of Cutaneous Reactions

(Hans Schmidt. Arch. f. Kinderh., 1910, liii, Nos. 4-6)

The author investigated the action of different food substances when applied to the skin as in a Pirquet test. The materials used were: 1. A substance composed of 40 per cent. meat extract, 20 per cent. egg albumen, 6.9 per cent. glycerin, salt and water. 2. A milk rich in fat, predigested with trypsin. The tests were made on 100 children suffering with different diseases. The reaction when positive resembled that of a positive Pirquet test. In 40 per cent. the reactions were positive. The influence of the different diseases on the determination of the reaction was not marked; the largest number of positive reactions was found in the case of functional neurosis and in the arthritic diathesis. The influence of age was, however, very marked, as shown by 20 per cent. of positive reactions in infancy as compared with 77 per cent. in patients over 10 years of age. It was found that a large number of those giving positive reactions had had several infectious diseases. Any direct relation between special diseases and positive reactions was not found.

G. L. Meigs.

Salt Fever and Excretion of Chlorin in Infancy

(Ragner Freiberger. Arch. f. Kinderh., 1910, liii, Nos. 1-3, p. 17)

The author gave eighty-three injections of salt solution to twenty children; a rise of temperature was noted after twenty-six injections in twelve of the children. In eight there was never any rise in temperature. His conclusions are that fever is often caused by the subcutaneous injection of salt solution, but this is very variable and uncertain; children suffering with nutritional disturbances more often show a rise in temperature than do normal children; the reaction seems to depend on the amount of salt given, 60 c.c. causing a reaction in 33 per cent., 10 c.c. in only 20 per cent.; there is no diminution in reaction caused by a repetition of the injections. Experiments were also made to determine whether there was a rise in temperature after the oral administration of salt; fifty-four experiments were made on eleven children; a reaction was present after eight experiments. Freiberger disagrees with the theory that the fever is caused by an action on the heat-regulating apparatus of the central nervous system, but thinks it probable that it may be caused by a reaction to some destructive change in the body cells caused by the salt. As to the excretion of chlorin in infancy, his conclusions are that salt injected subcutaneously is more slowly excreted than that taken by mouth; the excretion of salt is diminished in children suffering with nutritional disturbances or with the exudative diathesis.

G. L. Meigs.

METABOLISM AND NUTRITION

The Mineral Metabolism of a Healthy Breast-Fed Baby

(Tobler and Noll. Monatschr. f. Kinderh., 1910, ix, No. 4, p. 210)

In a six days' metabolism experiment on a healthy baby aged 2½ months, Tobler and Noll found that retention of the various salts in the body was as

follows: K_2O, 50.27 per cent.; Na_2O, 92.64 per cent.; CaO, 22.3 per cent.; Cl_2, 15.34 per cent.; P_2O_5, 56.51 per cent., and SO_3, 41.29 per cent.

FRITZ B. TALBOT.

Casein Milk in the Nutrition of Infants

(W. Birk. Monatschr. f. Kinderh., 1910, ix, No. 3, p. 140)

Birk fed thirty acutely or chronically sick babies with "Eiweiss-milch" (casein milk of Finkelstein and Meyer), which contains a low percentage of sugar and salts and a high percentage of casein. Five of the babies died soon or immediately after starting the use of the milk. A sixth was made worse by the food. Improvement in a child comes in the following way: first, a typical alkaline soap stool appears in place of the watery stool; the bacteria change from Gram negative to Gram positive. Most of the babies had no fever; in a few the giving of casein-milk was followed by a slight increase in the temperature. There was a gain in weight in some and loss in others. In the latter instance sugar should be added to the food. Birk concludes that casein-milk is valuable in some instances; is indicated in "acuten toxicosen" and in chronic digestive disturbances in which there is an intolerance for cow-milk fat. FRITZ B. TALBOT.

Some Questions of Human Milk Secretion, Especially Milk-Fat

(Dr. St. Engel. Arch. f. Kinderh., 1910, liii, Nos. 4-6)

The author investigated the amount of milk given by five wet-nurses at the different nursings during the day, all that was obtainable being taken at each feeding; 504 observations were made. His conclusions are: 1. The largest amount of milk was always given at the first feeding in the morning; less at the last feeding in the evening; during the day the amounts varied but were always less than those given in the morning and the evening. 2. The percentage of fat in the milk varied in inverse proportion to the amount; that is, it was least in the morning feeding, a little greater in the evening, greatest in the feedings during the day.

The second part of the investigation concerned the influence of diet on the percentage of fat in human milk. Contrary to the opinion of other investigators, especially Moll, St. Engel concludes that if the diet of a nursing woman is already sufficient, any addition of fat or other food stuffs has no effect on the percentage of fat. G. L. MEIGS.

Suitability of Condensed Milk for Infant Feeding

(James O. Jordan and Frank E. Mott. Am. Jour. Pub. Hyg., 1910, xx, 391)

An investigation was undertaken to determine whether the substitution of the common varieties of condensed milk for fresh milk and cream was founded on an economic basis and whether the substitute was suitable for infant feeding. Jordan and Mott first analyzed the milks as sold in the cans and from the results reckoned the fat in the original milk from which the condensed milk was made. The fat content was taken as the factor of chief importance because on it the commercial value of milk is calculated. They found that either milk of abnormally low grade was used or milk from which a portion of the cream had first been removed. The cost of condensed milk was then ascertained by determining the price per quart, provided it was diluted with only enough water to make the fat 3.35 per cent (the standard required by the Massachusetts law). The cheapest milk so made exceeds the price of ordinary milk and in some instances is more than the price of certified milk. If the dilutions advocated on the can are made the resulting mixture about equals a mixture of plain milk with one-third to equal parts of water. The greatest interest in this matter arises from the employment of condensed milk for infant feeding. If diluted as directed for this

purpose, the resulting mixture is an imitation of starvation diet. The manufacturers could not have advocated the employment of milk so diluted without being aware of its small food value. The formula from a common brand, the "Red Cross," for a baby 6 months old is, fat 0.84 per cent, sugar 1.41 per cent., cane sugar 4.30 per cent., proteids 0.87 per cent., carbohydrates 0.15 per cent., water 92.43 per cent. There is the further objection to the use of sweetened milks in the added cane sugar. Another fact of importance is that while a few of the brands were found sterile, a majority contained large numbers of organisms in many packages. The authors conclude that the only legitimate field for condensed milk is that of supplying a product where fresh milk is not available. The misleading statements by the manufacturers should be prohibited by law. Packages should bear a formula for diluting with water so that the resulting mixture shall not be below standard for milk solid or fat.

RICHARD M. SMITH.

Hypothyroidism in Nurslings and in Infants After Weaning

(*L. M. Spolverini. Revue d'hyg. et de méd. Inf., 1910, ix, No. 3, p. 201*)

Spolverini states that the signs of diminished thyroid secretion in infants do not appear until the end of the first year, or until after weaning. This he ascribes to substances furnished the child in breast-milk. He includes the mammary glands among the glands of internal secretion, influenced by the thyroid, and believes that diminished or increased thyroid secretion in the mother or nurse affects the nursling.

He divides infants into three groups: A. Those of a normal thyroid secretion, namely (1) mother or nurse and child with a normal thyroid; (2) mother or nurse with a normal thyroid and child with a hypo- or hyperthyroidism; (3) mother or nurse with a slight hypo- or hyperthyroidism and child with a normal thyroid. B. Those infants with a diminished thyroid secretion having for a determining cause the milk of the mother or nurse affected with insufficient thyroid secretion, and for predisposing cause a congenital hypothyroidism in the child. C. The group of infants with increased thyroid secretion, having for a determining cause the milk of a woman affected with hyperthyroidism, and for predisposing cause an unstable thyroid secretion, usually congenital in the child.

Spolverini deals entirely with children showing insufficient thyroid secretion and has studied in all nine patients, five of whom were still nursed and four already weaned. In addition four normal patients were used as controls. Thyroid extract was given in amounts, depending on the severity of the case and the age of the child, for periods of six days, followed by a day or more of rest. Nursing mothers, as well as the child, were given the drug. All patients showed a marked improvement; all gained weight, but those infants already weaned showed first a loss of weight. Improvement was most marked in the nursling whose mother or nurse received thyroid extract at the same time. All the controls showed a loss of weight during the treatment.

Heredity is the most important etiologic factor, and, of hereditary influences, disturbances of thyroid secretion in the mother hold first place. Other causes are alcoholism, tuberculosis, malaria and syphilis in either parent.

As the most important diagnostic signs in mild cases, in adults as well as children, he gives the following: the hard edema, often transitory; absence of the external third of the eyebrows; falling out or delayed appearance of hair; cold extremities; sensibility to cold; delayed dentition; constipation; anorexia; propensity to fatigue; headache; lack of muscular tone; pain in joints; apathy; drowsiness; absence of gain in weight, or occasionally, on the other hand, obesity; and retardation of mental and physical development.

In all these cases, mothers as well as children, an attempt was made by blood-serum tests to prove the variation of the complement while under treatment. This followed the line of work undertaken by Fassin, who found an increase in

the serum complement of thyroidectomized dogs and rabbits after the injection of thyroid extract.

In these cases Spolverini was unable to demonstrate any increase in the complement after the administration of thyroid extract. He did show, however, that the complement in the blood of the mother and of the nursling was nearly identical, but when the child was taken from the breast, the complement in the blood of the child showed a marked diminution from that of the mother.

J. HERBERT YOUNG.

Schematic Representation of Infant Feeding for Purposes of Instruction

(C. v. Pirquet. Ztschr. f. Kinderh., 1910, i, No. 1, p. 111)

Based on the fundamentals as taught by Camerer, Heubner, Czerny and Finkelstein, v. Pirquet shows by a series of figures the essentials of these new ideas.

Figure 1 represents the reactions of the normal child to increasing amounts of food. As indicated there is (1) a minimum, the smallest amount of the food necessary for the infant to gain weight; (2) an optimum, the amount it can handle with the greatest advantage; (3) a maximum, the tolerance limit, which is the greatest amount of the same food that the infant can take care of without drop in weight or bodily harm. The figure shows the loss in weight incident to passing either beyond the maximum or staying below the minimum. As long as the amount of food is kept within the nutritional range there can be no danger to the child *ex elimetitione*. The second figure, practically a continuation of the first, shows the effect of continued overfeeding, causing an acute intoxication with a gradual lowering of the tolerance until it falls far below the minimum. The food that in smaller amounts could have nourished the child acts like a poison when given in these large amounts.

Figure 3 shows the beneficial effect of reducing the food to a minimum, after over-feeding has produced a fat indigestion; explaining how with one-half the amount of the original food an infant can gain weight, when before it was standing still.

Figure 4 illustrates a more severe case of fat indigestion, in which reduction of the amount of milk is not sufficient, but the complete withdrawal of food is necessary to bring the tolerance back above the minimum, so that a large enough amount of food can be taken care of to produce a gain in weight.

Figure 5 represents the result of waiting too long in a case such as is illustrated in figure 4; the tolerance has been allowed to drop so low, that nothing can raise it above the minimum, which means that the child must die of inanition, because before sufficient of the food can be utilized to supply the waste it will act toxically.

Figures 6 and 7 show to a nicety what happens during an infection and during periods of high external temperature. The tolerance drops markedly and unless the food is reduced in the same measure gastro-intestinal disturbance will result.

Figure 8 illustrates the advantages of breast-milk in the therapy of gastro-intestinal disturbances. The tolerance limit is indicated for mother's milk one-half and one-third cow's milk. At point *a* the infant is exposed to high summer temperature, the tolerance for the food that it was taking falls far below the minimum, and only long days of starvation would bring it back within the nutritional range. By giving breast milk, however, a child can immediately be given quantities necessary to produce a gain in weight.

In Figure 9 v. Pirquet illustrates the relative low tolerance for cow's milk of the new-born infant, and its gradual rise with increasing age. The point at which the tolerance limit of a certain food crosses the minimum line, is the age at which the child can be raised with this food.

As v. Pirquet states, this contribution is a mere beginning, but a very excellent one, and one that will do much to make the teaching of the difficult subject of infant feeding a great deal easier than it has been heretofore.

H. F. HELMHOLTZ.

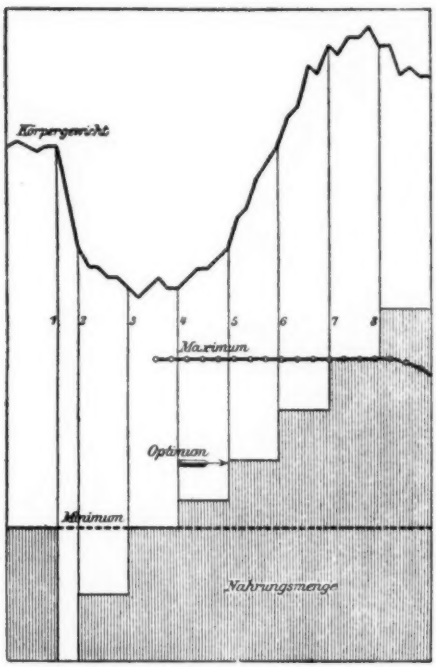

Fig. 1. Minimum, optimum and maximum of food.

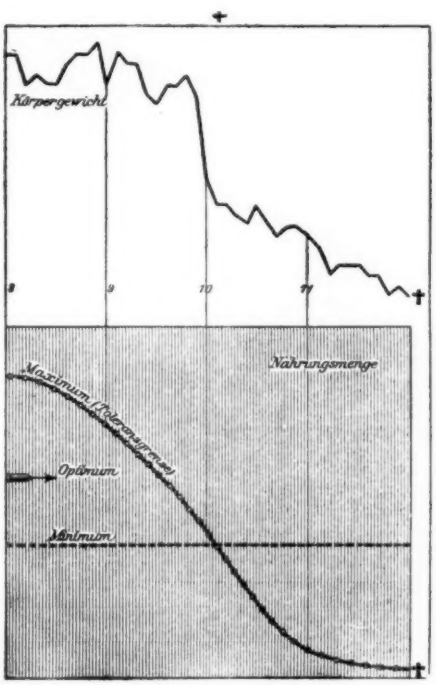

Fig. 2. Fatal gastro-enteritis due to over-feeding.

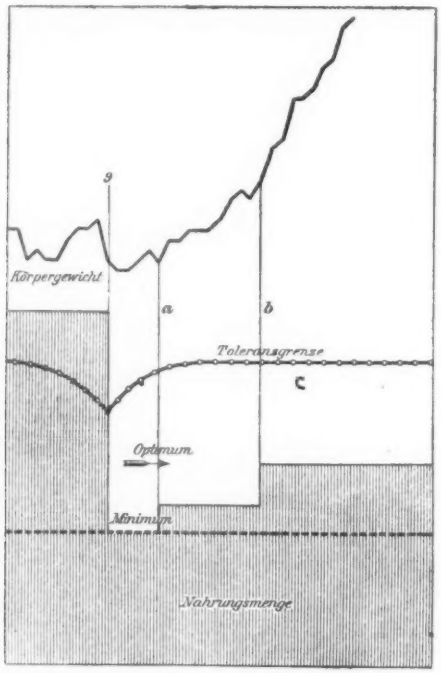

Fig. 3. Therapy in beginning fat-indigestion.

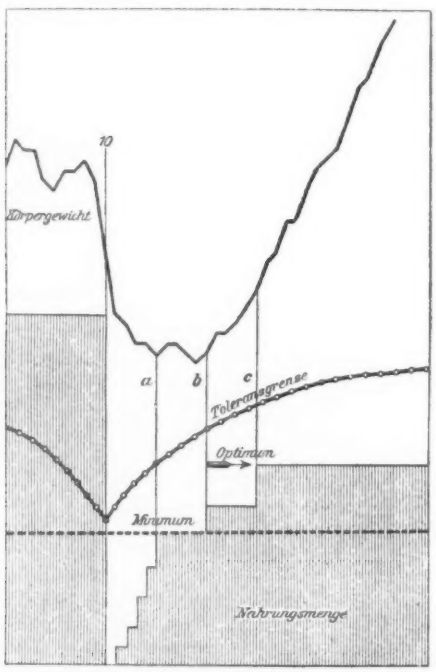

Fig. 4. Therapy in a more advanced case of fat-indigestion.

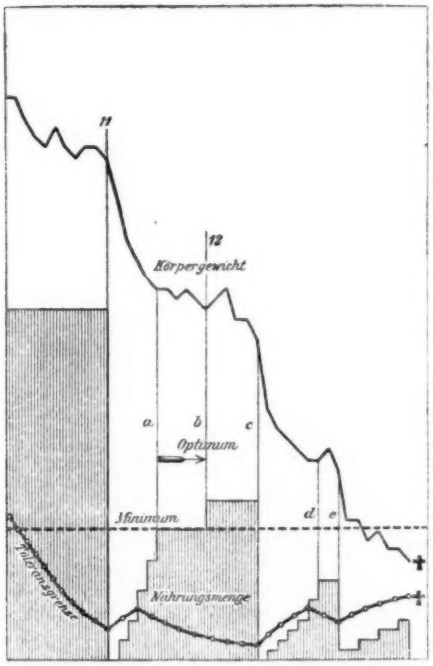

Fig. 5. Ineffectiveness of therapy when instituted too late.

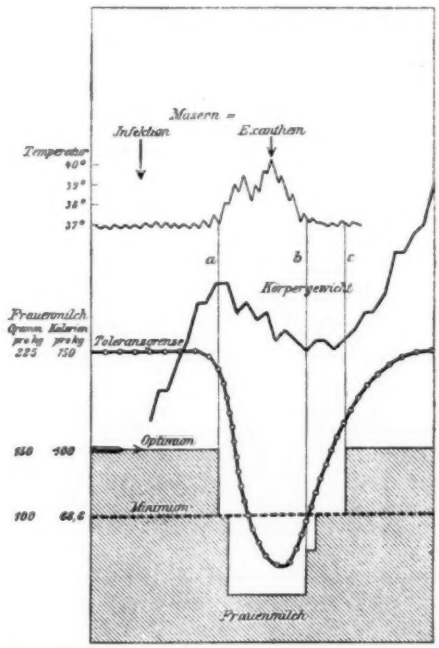

Fig. 6. Lowering of tolerance limit by an acute infection in a breast-fed child.

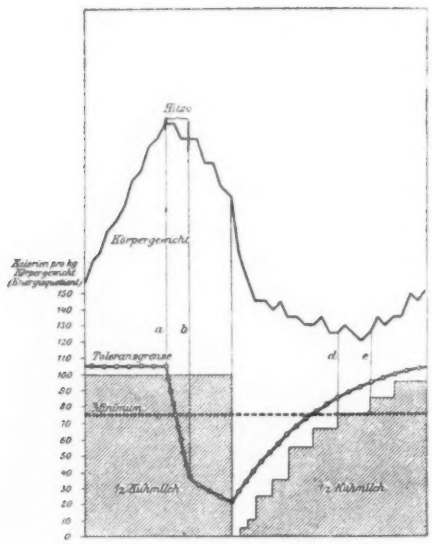

Fig. 7. Lowering of the tolerance limit by external heat in a bottle-fed child.

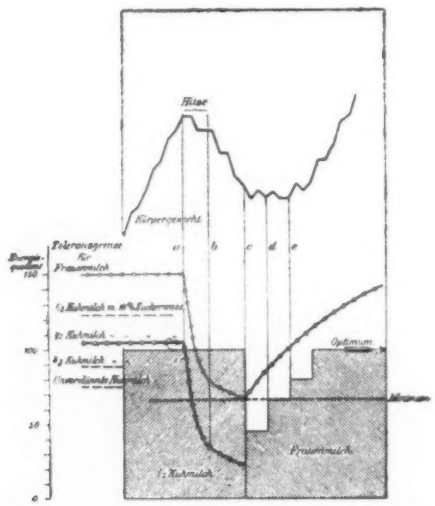

Fig. 8. Tolerance limits of a 6 weeks' old infant. The curing of an intercurrent disturbance by a return to mother's milk.

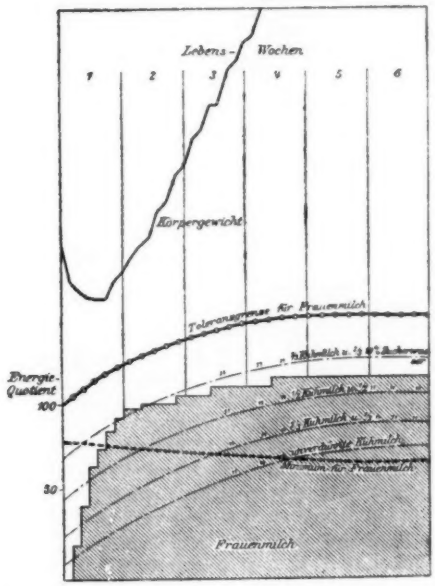

Fig. 9. Tolerance limits of a new-born infant and their gradual rise when breast-milk is fed.

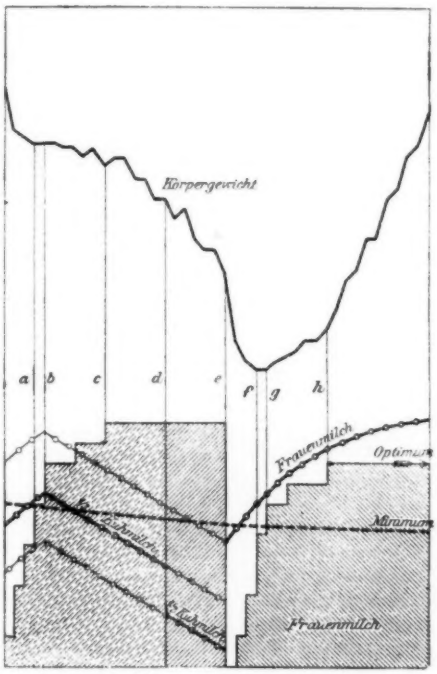

Fig. 10. Showing the effect of over-feeding with cow's milk in the new-born infant and improvement from breast-milk.

ACUTE INFECTIOUS DISEASES

Experience With 678 Tracheotomies During the Years 1899-1908

(J. C. Schippers, Amsterdam. Jahrb. f. Kinderh., 1910, lxxii, No. 5)

A study of these reports tends to show that intubation is not necessarily preferable to tracheotomy. The majority of the cases were diphtheritic laryngeal stenosis; almost invariably "tracheotomy inferior" was done, while a limited few had "tracheotomy superior." Anesthesia was seldom resorted to, and mostly in cases in which very strong children showed great resistance. One to 2 c.c. of chloroform sufficed as a rule, while very often the anesthesia due to the carbon dioxid was enough. All cases were first treated with antidiphtheritic serum, and also when possible with inhalations, ice-bags, warm baths, cold sprays, etc., to prevent the necessity of operation. The length of time necessary to wear the tube was interesting. While in 1899 the average length was five days, in 1908 it was 3.6 days. The time the 400 cases required nursing care averaged practically three weeks. The mortality in 492 cases, without lung complications preceding, was 18 per cent. Prognosis was of course clouded by lung complications, and by the duration of laryngeal stenosis; in the former it was 50 per cent. The mortality of patients operated on was no higher than that shown in intubation, and the latter method certainly has many more disagreeable features.

A. C. Soper, Jr.

New Views Regarding Treatment of Scarlatina

(G. Jochmann and G. Michaelis. Berl. klin. Wchnschr., 1910, xlvii, No. 20)

These authors regard the streptococcus as the chief factor of scarlatina, in spite of the fact that in a majority of the "foudroyant" fatal cases streptococci are not found. Their therapy is directed against the streptococcus by means of vaccines and serums. The serums of Marmorek, Aronson, von Leyden and others, tried in recent years, have been of no particular value. Then the Wright vaccine therapy was tried, controlled by the index technic in 130 cases, only establishing the fact that the index to streptococcus is low in scarlatina, and that it can be raised by opsonic therapy. No definite therapeutic benefit was seen. The serum was injected intravenously in the worst cases, those especially which had a bad prognosis from the first, and subcutaneously in the less severe ones. A combination of vaccine-therapy and serotherapy was tried in the majority of the 130 cases (in sixty-two, to be accurate). While the statistics here given did not prove anything definite, the authors feel warranted in regarding the treatment as a success, judging from considerable experience with it. The day of the injection seemed to make no difference. In a few cases injurious effects of the therapy were seen; eight had urticarial serum-exanthemata. No nephritis was found in thirty-eight patients who recovered. This therapy seemed of little or no avail in the severe cases, and was really of value only in those but slightly affected with streptococcemia.

A. C. Soper, Jr.

TUBERCULOSIS AND SYPHILIS

The Treatment of Tuberculous Children With Large Doses of Tuberculin

(A. Fuchs, Wien. Jahrb. f. Kinderh., 1910, lxxii, No. 5)

This work was begun in 1908 with treatment according to the Schlossman technic, and the dosage was generally with 1 gm. and upward; in each case a small dose if followed by no reaction was succeeded by a slightly larger one. No injections were given until the case was afebrile; then a start was made with 1 c.c. of a 1-1000 solution or less; if in forty-eight hours no febrile reaction ensued another injection was given, of twice the amount, and thus the technic proceeded by steps. If fever followed an injection, the next time the same dose was given—or a smaller one—and not until the case was afebrile was the original

dose returned to. As a rule, about two months was necessary to raise the dosage to 1 gm. Delay of the immunization process was seen in lung complications; an occasional case offered special resistance and an inconceivably small dose caused the worst reaction, so that finally the treatment was stopped. No improvement was seen in any case; in general the condition was made worse. In the method here used, no therapeutic effect was seen in the surgical cases; in some cases, indeed, an exacerbation of the disease was seen, with propagation to other parts of the body. The same was true of pulmonary tuberculosis. Peculiar anaphylactic skin reactions occurred with great regularity in "local" injections.

A. C. Soper, Jr.

Colles' Law and the New Syphilitic Facts

(*W. Knopfelmacher and H. Lehndorf. Jahrb. f. Kinderh., 1910, lxxi, No. 2*)

This work deals with the question whether hereditary syphilis is a placental or a germinal transmission of infection, helping to clear up the theories on the basis of the discovery of the specific microorganism. Matzenauer and others discussed this fully, earlier, and seem to have decided more in favor of a placental than a germinal transmission. Three points are considered: 1. Inflammatory changes in the placenta and umbilical cord are very common even if not pathognomonic. 2. Spirochetes are found in the fetal parts, and especially in the fetal ovaries and testicles, although not yet demonstrated in such parts in the adult. Of especial interest is the finding of the spirochete in the placenta—seldom in the maternal parts, but more generally in the fetal; nevertheless, no sure conclusions are possible as to the exact origin of hereditary syphilis. 3. The Wassermann reaction was positive in 62 per cent. of 116 women whose children had hereditary syphilis. These were divided into two groups, of whom the first had not shown demonstrable syphilis and the second had; group 1 had 59 per cent. positive and group 2 had 72 per cent. They conclude that the mothers of syphilitic children, whether denying syphilis or not, showed practically the same response to the Wassermann. Also, the number of births of syphilitic children per woman was no factor; only women bearing eight or more showing a lower per cent. (46 per cent.). The percentage varies from 90 per cent. positive in women examined a short time after the birth of a syphilitic child, to 40 to 50 per cent. of those examined many years after such births. Probably all such react the same as syphilitic patients. Also, syphilis is believed to be transmitted by and from the mother, and not by paternal germination. The evidence that without exception all children with hereditary lues are infected *ex matre* and by the placental route stands fast and is not to be confuted; and the possibility of a paternal origin must be regarded with greater incredulity than before.

A. C. Soper, Jr.

Hereditary Syphilis and the Wassermann Reaction

(*P. Mulzer and W. Michaelis. Berl. klin. Wchnschr., 1910, xlvii, No. 30*)

The patients chosen were all syphilitic, or supposed to be; the majority were infants (excluding new-born); forty-four patients with manifest syphilis showed forty-two positive and two negative Wassermann reactions. Also, in fresh congenital syphilis, 95 per cent. were positive. In this last group were three especially interesting cases; one, a child 2 months old, had given a negative Wassermann reaction three weeks before the outbreak of the syphilis, i. e., while it yet showed no syphilitic symptoms. The serologic examination was made because the mother had rigid pupil-reflex and the father was in an insane asylum with cerebral softening. In this case with the onset of syphilitic symptoms came the first positive reaction. The same was true of a second patient whose two older sisters were syphilitic and who nevertheless showed no symptoms; at first negative, the reaction was positive only later, when a coryza had begun. A third patient was examined because it was a 7 months' birth and the father was syphilitic. The serum reaction was positive although no syphilitic symptoms were present. The cases of latent hereditary syphilis were equally

interesting. Positive reaction was found in 59 per cent. Referring to the patients treated, it could not be demonstrated that a negative reaction was produced; of nineteen patients only six showed first a positive and later a negative reaction. Conclusions: of mothers of syphilitic infants 90-100 per cent. react positively; this is also true of women who within four years have borne syphilitic children. Also, symptomless children of syphilitic mothers, showing negative reaction shortly after birth, show a positive reaction a few weeks later, and mostly at the onset of syphilitic symptoms. A. C. SOPER, JR.

GASTROINTESTINAL SYSTEM

Bacteriology of Bacillary Dysentery

(*A. L. Kendall. Boston Med. and Surg. Jour., 1910, clxiii, 398*)

Kendall states briefly the principles underlying the activity of the dysentery bacillus as associated with the disease, bacillary dysentery. The foundation for the work rests on these principles: 1. Bacteria in presence of protein and fermentable carbohydrate act on carbohydrate, in the vast majority of cases attacking the protein only sufficiently to satisfy their nitrogen requirements. 2. In the body carbohydrate also can be used to prevent metabolism of nitrogen. 3. Dysentery bacilli attack fermentable carbohydrate in preference to protein. 4. Bacteria attacking protein form toxic putrefactive products, but not if grown in media containing carbohydrate which they can utilize. The products of the dysentery bacillus which are harmful are largely protein decomposition products and can be prevented by utilization of sugar instead. 5. The blood of normal human beings contains about 0.2 per cent. dextrose. 6. The normal sugar for man is lactose, an animal sugar. It is utilizable by few bacteria except those of intestinal origin. The bacterial flora of the intestinal tract in bacillary dysentery is putrefactive, because of the small amount of sugar present. This is also true within the body, for the dextrose is early used up, especially if the patient is on starvation diet. The remedy, bacteriologically speaking, is to add an excess of sugar to the intestinal tract and restore the normal amount of dextrose to the blood. Chemically pure dextrose can be supplied in 2.5 per cent. strength in normal saline solution, given subcutaneously. This furnishes fuel to be used immediately by the body and also food for the invading organisms, thus sparing the body tissue. Feeding lactose by mouth (5 per cent. solution) brings about a similar change in the intestinal bacteria, converting a putrefactive into a fermentative type and producing lactic acid, an antagonist to the dysentery bacillus. Coincidently with this change the intestinal flora approaches that of normal infants—*B. bifidus* and *B. acidophilus* begin to appear in the stools. These organisms also produce lactic acid, still further antagonizing the dysentery bacillus.

RICHARD M. SMITH.

CIRCULATORY SYSTEM

Blood-Pressure in Childhood

(*Fr. Wolfensohn-Kriss. Arch. f. Kinderh., 1910, liii, Nos. 4-6.*)

The author studied the blood-pressures of 350 children in order to determine the normal blood-pressure, and the influence on it of age, size and weight. The children varied in age from a few weeks to 14 years and the blood-pressure from 80 to 113 mm. of mercury.

The author's conclusions are: 1. The blood-pressure increases in direct proportion to the age, size and weight. 2. Age alone has no influence on the blood-pressure, which depends rather on the size and weight. 3. Sex has no influence on blood-pressure, provided size and weight are the same. The author also studied the blood-pressure of sixty-five sick children, but found that the number was too small to allow of any conclusions. In eight cases of tuberculosis, and in ten cases of bronchitis the blood-pressure was normal for the age. G. L. MEIGS.